A Partnership for Health:

Minorities & Biomedical Research

The National Institute of
Allergy and Infectious Diseases
U.S. Department of Health
and Human Services
National Institutes of Health

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Foreword

As we prepare to enter the 21st century, NIAID looks back upon 50 years of progress in understanding, treating, and preventing infectious and immunologic diseases. However, despite the scientific breakthroughs and medical advances, not all of our citizens are reaping the benefits of this increased knowledge. This has made the reduction of these health disparities a national priority.

Health disparities, whether they be due to differences in incidence, prevalence, mortality, or burden of disease, continue to exist among the various minority and ethnic groups that comprise our society. Those who suffer and the health professionals who treat them have long recognized these disparities. In some instances these disparities are continuing to occur although medical science progresses and new public health programs are being focused on them. This pamphlet highlights not only the strides that have been made by NIAID in its scientific research endeavor, but also reflects our efforts to ensure that all members of our society are adequately represented in the patient populations of the clinical studies we undertake. We are highly cognizant of the diseases that seem to disproportionately affect these populations and seek various means to attract researchers to conduct studies into their cause and to find treatment modalities to minimize their toll.

While some of the causes of inequitable health outcomes may be beyond the mission of NIAID and NIH, we will continue to put all our efforts into addressing those areas that do fall into the realm of biomedical research and meet the Department of Health and Human Services' Healthy People 2010 initiative to reduce health disparities.

Anthony S. Fauci, M.D.
Director
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Executive Summary

Minority populations in the United States bear a disproportionate burden of sickness and disease. Many of these health problems fall within the purview of the National Institute of Allergy and Infectious Diseases (NIAID), which include acquired immunodeficiency syndrome (AIDS), asthma, sexually transmitted diseases, tuberculosis, autoimmune diseases, and kidney disease. NIAID has developed a comprehensive program of basic, clinical, and epidemiologic research designed to reduce the severity and prevent the occurrence of these and other conditions.

The Institute strives to include individuals from minority populations in all phases of its research program, from the recruitment of patients for clinical trials to the involvement of minority researchers. NIAID also is resolved to increase the number of minority scientists by supporting undergraduate, graduate, and postgraduate research training in immunologic and infectious diseases.

Asthma morbidity and mortality have been increasing in the United States for the past 15 years and are particularly high among poor African American and Hispanic/Latino inner-city residents, especially children. In response to the recent rise in asthma morbidity among nonwhite populations, NIAID launched the National Cooperative Inner-City Asthma Study to isolate the causes for this increase and to develop self-management strategies to reduce or eliminate the severity of the attacks. We are now entering the second tier of this study to evaluate the effectiveness of the intervention strategies developed during the first-tier study.

NIAID supports 13 Asthma and Allergic Diseases Research Centers to carry out multifaceted basic and clinical research projects on the mechanisms of asthma and allergic diseases as well as treatment and prevention strategies. These centers are located in rural and urban sites throughout the United States.

Autoimmune diseases such as systemic lupus erythematosus and insulin dependent diabetes mellitus affect the African American population disproportionately. In collaboration with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Institute of Child Health and Human Development (NICHD), NIAID is supporting the Diabetes Prevention Trial-Type 1, the first large nationwide trial of an immunomodulatory agent for the prevention of an autoimmune disease.

In 1999, NIAID awarded grants to establish four Autoimmunity Centers of Excellence. These centers will incorporate a clinical component into research efforts that focus on understanding the defect in self-tolerance observed in autoimmune disease. This research initiative will yield the piloting of novel immune therapies for these diseases.

NIAID's microbiology and infectious diseases segment of its scientific agenda includes intramural and extramural research to control and prevent diseases caused by virtually every infectious agent. One of the Institute's primary goals is to extend the impact of vaccines in preventing disease. Since 1981, NIAID has supported a program to accelerate the development of new vaccines.

For example, NIAID has dramatically increased funding for TB research during recent years, from approximately $3.5 million in 1991 to approximately $40 million in 1999. This increased funding has allowed the Institute to fund a number of initiatives and a markedly increased community of TB researchers. It has also enabled NIAID to continue its support of the Tuberculosis Research Unit (TBRU) for an additional 7-year contract period.

In collaboration with the National Heart, Lung, and Blood Institute (NHLBI), NIAID is funding an initiative to support the development of improved animal models for TB, particularly in the areas of per-

sistence and reactivation of disease because most cases of TB arise in persistently infected individuals (roughly 2 billion people, globally). In collaboration with the Fogarty International Center, NIAID is supporting seven new supplemental training awards to improve global health research and public health capacity for response to the TB epidemic.

During 1998, approximately 75 percent of the active cases of TB were reported among racial and ethnic minorities. The disproportionate impact of TB among minorities is related to many socioeconomic factors, such as overcrowded living conditions, HIV infection, and inadequate treatment and/or compliance with TB chemotherapy.

NIAID presented a *Blueprint for TB Vaccine Development* at the 1998 International Symposium for Tuberculosis Vaccine Development and Evaluation. The *TB Blueprint Report* outlines the specific steps needed to develop improved TB vaccines. A trans-DHHS Task Force, which includes representation from NIAID, will oversee implementation of the *TB Blueprint Report*.

The current epidemic of sexually transmitted diseases (STDs) in the United States disproportionately affects minorities. A high priority at NIAID, STD research emphasizes the impact of STDs on women and the relationship between STDs and HIV infection. The Institute's ongoing efforts in STD research include funding seven STD Cooperative Research Centers (CRC) and six program project grants to develop topical microbicides.

In 1998, 64 percent of the 14 million cases of STDs occurred in people younger than 24 years of age. More than 3 million of these cases occurred in teens. NIAID currently has several STD research activities to address the increasing problem of STDs and adolescents. In collaboration with the Rockefeller Foundation, the Institute is compiling and editing a monograph on adolescents and STDs. NIAID has awarded a STD CRC devoted to research in adolescent populations and has an additional four large-scale clinical studies in progress that focus specifically on minority adolescent populations.

Emerging infectious diseases may pose a continuing or even growing threat in the United States in coming years. NIAID supports basic and applied research on the causes of and treatments for infectious diseases and has developed a Research Agenda for Emerging Infectious Diseases to provide an integrated and proactive research strategy to address this problem. As part of this agenda, NIAID supports four Hepatitis C Cooperative Research Centers, which conduct basic and clinical research studies.

In collaboration with an expert panel, NIAID has developed a *Framework for Progress for Hepatitis C*. This document defines the major basic and clinical research objectives, questions, and resources needed to achieve the Institute's research goals related to hepatitis.

Today, racial and ethnic minorities account for more than 60 percent of the reported AIDS cases in the United States. The majority of HIV-infected women (80 percent) are among African American or Hispanic populations. As a consequence, the majority of HIV-infected children are African American or Hispanic/Latino. NIAID addresses minority issues in HIV disease in four major areas: treatment research, epidemiologic research, vaccine and prevention research, and infrastructure development and training of minority researchers.

The NIAID national clinical trials program includes the Adult AIDS Clinical Trials Group, the Pediatric AIDS Clinical Trials Group, and the Terry Beirn Community Programs for Clinical Research on AIDS. All of these networks strive to ensure that a sufficient proportion of minority subjects is enrolled into clinical trials so that the results of the research may be generalizable to the affected HIV population at large. NIAID-supported epidemiology studies include the Women and Infants Transmission Study and the Women's Interagency HIV Study, which operates in tandem with the Multicenter AIDS Cohort Study. Enrollment of people of minority background in these studies is 86 percent, 80 percent, and 15 percent, respectively.

The HIV Network for Prevention Trials (HIVNET) has a broad-based agenda that includes trials of vaccines, topical microbicides, STD treatment, behav-

ioral interventions, and approaches to prevent mother-to-infant transmission. The HIVNET Vaccine Preparedness Study is evaluating strategies for conducting future HIV vaccines and other preventive measures in populations at greater risk for contracting HIV in the United States.

In February 1999, the first NIAID-supported AIDS vaccine trial in Africa was initiated in Uganda. This study will help investigators determine if customized vaccines are necessary for different parts of the world. Another international vaccine trial is slated to begin in early 2000 in Brazil, Haiti, and Trinidad. Furthermore, international studies to evaluate non-vaccine interventions are currently underway in more than 20 developing countries.

NIAID is developing an AIDS vaccine communication campaign to increase awareness of AIDS vaccine research before the initiation of an efficacy study. Part of this campaign will include developing messages that will promote and enhance the participation of high-risk communities, including minorities, in NIAID-sponsored vaccine trials.

NIAID research results are disseminated to underserved minority communities through the Institute's outreach activities. The Institute has recently updated its nine fact sheets on sexually transmitted diseases other than HIV/AIDS. This series covers pelvic inflammatory disease (PID) and syphilis, which affect a disproportionate number of minorities.

NIAID has responded to a critical need for patient information on TB by publishing easy-to-read booklets in English and Spanish titled *Learn About Tuberculosis* and *Learn About Tuberculosis Infection*.

The Institute helps support a new NIH Spanish-language newsletter, *El Pulso de la Salud: Información de los Institutos Nacionales de la Salud*, which is distributed nationwide. NIAID serves on the NIH committee that publishes the newsletter and contributed articles on HIV/AIDS and sexually transmitted diseases in its first two editions.

In October 1999, NIH launched a major Curriculum Supplement Series for kindergarten through grade 12. NIH will distribute the series to teachers throughout the United States free of charge to improve science literacy and to foster students' interest in science. NIAID's contribution to the curriculum is called *Emerging and Re-Emerging Infectious Diseases*, which targets grades 9 through 12.

The Institute's outreach efforts also seek to expand recruitment of minority populations into clinical trials, including a trial on diabetes, which affects African Americans and Native Americans at higher rates than other populations.

Increasing the participation of underrepresented minority investigators in virtually all fields of biomedical research is a continuing NIH and NIAID priority. NIAID supports a variety of minority programs for biomedical research, encompassing high school through postdoctoral training.

In January 1998, NIAID created the Office of Special Populations and Research Training (OSPRT). OSPRT combines the functions formerly housed in the Office of Research on Minority and Women's Health with those under the Office of Science Training and Manpower Development. OSPRT administers the Bridging the Career Gap for Underrepresented Minority Scientists Workshop and the Introduction to Biomedical Research Program (IBRP) as well as many other unique programs. In addition, OSPRT is actively involved in various collaborative funding efforts between NIAID and the NIH Office of Research on Minority Health and the NIH Office of Research on Women's Health.

In 1999, NIAID sponsored its fourth Bridging the Career Gap for Underrepresented Minority Scientists Workshop, which was established in 1993 to nurture the careers of young minority investigators currently funded by the Institute under various minority training and research supplemental awards.

Also in 1999, the Introduction to Biomedical Research Program (IBRP) celebrated its 20th anniversary. This program was established to inform academically talented college juniors, graduating seniors, and first-year graduate or medical students

from underrepresented minority groups about career opportunities in the broad field of biomedical research. This initiative grew out of the need to increase the number of minority scientific researchers in the United States.

Twenty years later, NIAID is beginning to see the long-term effects of this innovative program. Several IBRP participants have received NIH grants, been tenured in academia, entered the Institute's intramural training programs, and joined the extramural staff.

NIAID recognizes that it must not only maintain but also expand its commitment to improve minority health and attract more capable minority researchers to allergic and infectious disease research. A healthy citizenry is an essential part of a productive society. NIAID will continue its efforts to increase the participation of ethnic minorities in its crucial research agenda and seek to eliminate health disparities wherever they occur in our nation's population.

I. Minority Health Initiatives

Allergy, Immunology, and Transplantation

The National Institute of Allergy and Infectious Diseases (NIAID) supports research that focuses on enhancing an understanding of the role of the immune system in the pathogenesis, treatment, and prevention of many immune-mediated diseases, including asthma and allergies; autoimmune disorders, such as diabetes mellitus (type 1) and systemic lupus erythematosus (SLE); and the transplantation of solid organs for the treatment of end-stage organ failure. NIAID seeks to improve the health status of the Nation's minority populations through support for basic and clinical research, demonstration and education research projects, and minority health resource development.

NIAID's objectives with respect to minority health in the areas of allergy, immunology, and transplantation are threefold: First, to support basic and clinical research directed at certain health problems as they affect minority populations, e.g., asthma, SLE, and end-stage kidney disease; second, to support demonstration and education research aimed at reducing the severity or incidence of certain health problems among minorities through the design and testing of the effectiveness of interventions; and third, to increase the number of minority biomedical scientists through individual and institutional support for undergraduate, graduate, and postgraduate research training in a variety of disciplines relating to disorders of the immune system.

Asthma and Allergic Diseases

Immunologic diseases affect millions of Americans resulting in considerable morbidity, mortality, and medical costs. Those immune-mediated diseases most readily known by the majority of Americans are asthma and allergies. More than 50 million Americans, 1 out of every 5, are reactive to at least 1 of 8 selected allergens known to contribute to allergic illness.

Asthma is an inflammatory lung disease. The cellular infiltrates and inflammatory mediators of asthma are thought to be similar to those of other allergic diseases, but the mediators apparently also cause airway hyperactivity. While allergic reactions are an important cause of asthma, non-immunologic factors, such as viral infections and exposure to environmental tobacco smoke and pollutants, also contribute to the pathophysiology of this disease.

Asthma causes significant morbidity and enormous economic costs. Asthma morbidity and mortality have been increasing in the United States for the past 15 years, and asthma morbidity and mortality is particularly high among poor, African American inner city residents. Low socioeconomic status, exposure to cockroach allergens and pollutants, lack of access to medical care, and lack of self-management skills all contribute to increased morbidity from asthma.

In 1994, the prevalence of asthma was estimated to be 14.6 million persons (approximately 5.6 percent of the population) in the United States, of which nearly 4.8 million were children ages 17 years or younger (6.9 percent); and asthma was the first-listed diagnosis for more than 468,000 hospitalizations. Asthma is more prevalent among African American children who are 6 to 11 years old than among white children of the same age (9.4 and 6.2 percent, respectively). The prevalence of asthma increased approximately 40 percent among U.S. children under 18 years of age during the decade of the 1980s. Although asthma deaths are infrequent, mortality rates for all ages increased 46 percent during the 1980s (1.3 per 100,000 or 2,891 deaths to 1.9 per 100,000 or 4,867 deaths). Between the ages of 0 to 24 years of age, asthma deaths increased 118 percent between 1980 and 1993. Among 5- to 34-year-olds, nonwhites were two to three times as likely as whites to die from asthma.

Although asthma is a disease with low mortality, its economic costs are enormous with an estimated cost in the United States in 1990 of $6.2 billion. The largest single indirect cost was $1 billion for decreased productivity due to loss of school days. Despite the widespread assumption that asthma is a mild illness, 43 percent of the cost was due to emergency room use, hospitalization, and death. In 1994, the latest year for which there are data, asthma accounted for 134 million days of restricted activity and 64 million days of bed disability.

In response to this rise in asthma morbidity in inner city children, NIAID initiated the National Cooperative Inner-City Asthma Study (NCICAS) in FY 1991. NCICAS was composed of eight study units that engaged in a seven-city study aimed at improving morbidity of asthma among inner-city children. The sites were located in New York City (2); Washington, D.C.; Baltimore; Chicago; Cleveland; Detroit; and St. Louis. The study was conducted in two phases.

Phase I, which ran from November 1992 to June 1994, had the objective of identifying interventional factors related to asthma severity and morbidity among inner-city children. Phase I recruited approximately 1,500 children ages 4 to 9 years from emergency rooms and primary care clinics within the eight metropolitan areas. The population was approximately 20 percent Hispanic American and 73 percent African American, with the remainder white. The participants in this cohort experienced a high level of asthma morbidity. The participants underwent a comprehensive examination, which included pulmonary functions, allergen skin tests, and urinary cotinine to monitor exposure to environmental tobacco smoke. Information was collected on asthma severity, access to health care, compliance with medical therapy, psychosocial issues, living conditions, and the economic cost of asthma treatment. More than 90 percent of the participants were followed at 3-, 6-, and 9-month intervals to monitor asthma morbidity prospectively. Home environmental surveys, which measured allergen exposure (dust mite, cat, cockroach) and home nitrogen dioxide levels, were completed in more than 660 homes.

Results from phase I yielded the following:

- Knowledge about asthma is high, but asthma self-management skills are poor.

- Cockroach may be the most important allergen among inner-city children with asthma. Cockroach allergen levels are high, and a higher proportion of inner-city children are sensitive to cockroach than to dust mite and other allergens. In contrast, cockroach is a minor allergen in children with asthma who live in the suburbs.

- Asthma severity correlates with the degree of cockroach sensitivity and sensitivity in turn correlates with the levels of cockroach allergen exposure.

Based on these findings, NIAID began phase II, which ran from November 1994 to January 1996. This phase of the study was designed to evaluate the cost-effectiveness of an asthma counselor in reducing the excessive burden of asthma morbidity. The intervention recruited 1,033 inner-city children with asthma, ages 5 to 11, and their families to participate in the phase II intervention.

This second phase of NCICAS evaluated a broad-based, comprehensive educational, behavioral, and environmental intervention to improve asthma in inner-city children. The participating children, suffering from moderate to severe asthma, were selected from eight metropolitan sites: Baltimore, Bronx, Chicago, Cleveland, Detroit, New York, St. Louis, and Washington, D.C. The racial make-up of the children was African American (78 percent), Hispanic (16 percent), and Caucasian (6 percent). Three of the phase II sites adopted the intervention strategy to use with Spanish-speaking children.

The intervention, which was tested over a 1-year period, demonstrated the utility of an asthma counselor to assist each family in managing the child's condition, coupled with environmental controls in the home. This highly successful program reduced major asthma symptoms, hospitalizations, and emergency room visits by about 30 percent. Remarkably, those improvements were maintained during a second year follow-up without the assistance of an asth-

ma counselor, suggesting that the intervention allowed the children and their families to acquire self-management skills of long-term benefit to their asthma.

One very notable success of this study was the recruitment of large numbers of children, and the high retention rate. Fully 93 percent of those recruited completed the study including the intervention. This unique success can be attributed, in large part, to the expertise and effort on the part of the researchers to ensure high retention through a stable study infrastructure and monitoring system.

In 1996, NIAID and the National Institute of Environmental Health Sciences (NIEHS) launched a multi-center, 5-year study to refine and evaluate NCICAS-I with particular emphasis on the environmental components. The study, called the National Cooperative Inner-City Asthma Study II, is being conducted at seven clinical centers located in Boston, Bronx, Chicago, Dallas, New York, Seattle, and Tucson, with a data coordinating center in North Carolina. This study has successfully recruited 950 children with asthma, ages 5 to 12, to test the effectiveness of two interventions aimed at reducing the severity of their asthma.

This NIAID/NIEHS-sponsored Inner-City Asthma Study has also initiated an additional protocol, being funded by the Environmental Protection Agency (EPA), to monitor indoor and outdoor pollutants in each of the clinical study cities and has selected homes at each study site.

NIAID is collaborating with the American Academy of Allergy, Asthma, and Immunology, and other professional allergy organizations on a task force for clinical practice guidelines for allergic diseases and asthma. This task force is charged with developing evidence-based guidelines for the diagnosis, management, and prevention of allergic diseases and asthma. The executive summary was published in FY 1999 and the guidelines should be available in FY 2000.

In late 1998, NIAID issued a Request for Applications (RFA) for its Asthma and Allergic Diseases Research Centers initiative. The centers conduct multi-component projects consisting of basic and clinical studies focusing on mechanisms of, and treatment and prevention of, asthma and allergic diseases. In FY 1999, NIAID supported a total of 13 centers. These centers are located across the United States and include rural as well as urban sites.

The biannual meeting of the directors of NIAID-sponsored asthma centers was held at NIH on June 10-11, 1999. This meeting was co-sponsored by NIAID and NIEHS. The presentations focused on an update of the Inner City Asthma Study, and of the role of allergens and pollutants in asthma and allergy, the causes of asthma in early life, and the future of allergen immunotherapy. Both academic and industry investigators participated in the meeting.

NIAID, along with other institutes and agencies of the Department of Health and Human Services (DHHS), is participating in a DHHS-sponsored work group on asthma. This work group is charged with identifying unmet needs and opportunities in asthma research, surveillance, and public health practice, and with developing a planning document for asthma research that will be used as a resource for DHHS Secretary Shalala and program staff at DHHS. The working group has produced a draft document titled *Action Against Asthma: A Strategic Plan for the Department of Health and Human Services*. The draft can be accessed at the following web site: http://aspe.os.dhhs.gov/sp/sphome.htm.

The President's Task Force on Environmental Health Risks and Safety Risks in Children, which is co-chaired by Secretary Shalala and Carol M. Browner, EPA, has identified asthma as a priority area and established an Asthma Priority Work Group in which NIAID has been an active participant. The Asthma Priority Work Group is charged with developing an initiative focusing on environmental influences on asthma in children. The asthma initiative includes components of research, surveillance, and public health practice. The asthma initiative is being developed parallel with the DHHS Asthma Initiative. The Asthma Priority Work Group has produced a document titled *Asthma and the Environment: A Strategy to Protect Children*, which

can be accessed online at the following web site: http://www.health.gov/environment/fin.pdf.

The General Accounting Office (GAO) has prepared a report on research activities supported by EPA and other governmental agencies, including NIAID and several other institutes of NIH. This report will be used to develop an integrated, cost-effective research plan to be used by these Government agencies to address gaps in the current understanding of health risks, especially for asthmatics, posed by indoor pollution, including indoor allergens.

In March 1999, the National Library of Medicine (NLM), in collaboration with NIAID, NIEHS, and the National Heart, Lung, and Blood Institute (NHLBI), opened an exhibition titled *Breath of Life*. This exhibit highlights the history of asthma, the experiences of people with asthma, and contemporary research and management efforts to control the disease.

The forthcoming publication of *Healthy People 2010*, being developed under the aegis of the DHHS Office of Disease Prevention and Health Promotion, will contain goals for increasing years and quality of life for our Nation's citizens and for the elimination of racial and ethnic health disparities as well. NIAID is participating in the preparation and editing of the section on asthma in the chapter on lung diseases. Participants in the development of this chapter also include NHLBI, NIEHS, and the Centers for Disease Control and Prevention (CDC).

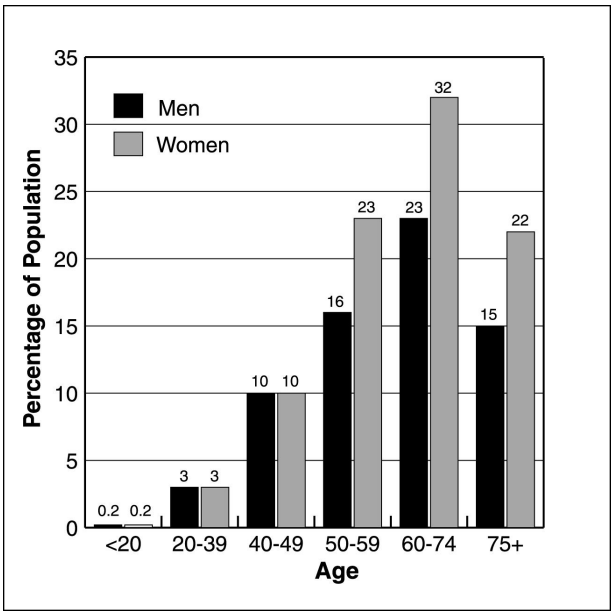
Autoimmune Diseases

The autoimmune disorders can be divided into two main groups: organ specific and non-organ specific diseases. Organ-specific diseases are characterized by immune reactions and tissue damage localized to a single organ or tissue. For example, in type 1 diabetes mellitus the damage occurs in the islets of Langerhorns located in the pancreas, and for multiple sclerosis the associated scarring occurs on the spinal cord, which affects the central nervous system. In contrast, non-organ specific diseases such as systemic lupus erythematosus (SLE) are characterized by immune reactivity against antigens distributed throughout the body resulting in widespread tissue damage.

Type 1 diabetes mellitus affects between 300,000 and 500,000 persons in the United States, of which 120,000 are 19 years of age or younger. This disease results in 484,000 hospitalizations per year and 12.8 million physicians' office visits annually.

About one-third of total diabetes cases are undiagnosed among African Americans and Hispanic Americans. This is similar to the proportion for other racial and ethnic groups in the United States.

Figure 1. Prevalence of diagnosed and undiagnosed diabetes in African Americans, U.S., 1988-1994.



Note: Diabetes includes both previously diagnosed dia - betes and undiagnosed diabetes (fasting plasma glucose greater than 126 mg/dL).

Figure 1 shows the prevalence for African American men and women based on the most recent national study, the NHANES III survey conducted from 1988 to 1994. The proportion of the African American population that has diabetes rises from less than 1 percent for those younger than 20 years of age to as high as 32 percent for women ages 65 to 74. In every age group, prevalence is higher for women than men. Overall, among those 20 years or

older, the rate is 11.8 percent for women and 8.5 percent for men.

National health surveys during the past 35 years show that the percentage of the African American population that has been diagnosed with diabetes is increasing dramatically. The surveys in 1976-1980 and in 1988-1994 measured fasting plasma glucose and thus allowed an assessment of the prevalence of undiagnosed diabetes as well as of previously diagnosed diabetes. In the earlier survey, total diabetes prevalence in African Americans among 40-to 74-year olds was 8.9 percent; in the latter, total prevalence had increased to 18.2 percent—a doubling of the rate in just 12 years. Prevalence in African Americans is much higher than in white Americans. Among those aged 40 to 74 in the 1988-94 survey, the rate was 11.2 percent for whites, but was 18.2 percent for African Americans—diabetes prevalence in African Americans is 1.6 times the prevalence in whites.

Mexican Americans represent the largest Hispanic American subgroup, comprising 64.3 percent of the Hispanic population in the United States. Central and South Americans represent the second-largest Hispanic American subgroup, with 13.4 percent of the Hispanic population. The majority of Hispanic Americans live in the south-central and southwestern United States. Table 1 provides a list of Hispanic subgroups, the percentage of the total Hispanic population they each represent, and the percentage of the population that has diabetes for two age ranges. The proportion of the Mexican American population that has diabetes rises from less than 1 percent for those younger than 20 years of age to as high as 33 percent for women ages 60 to 74. As with the African American population, in almost every age group, prevalence is higher among women than men.

In collaboration with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Institute of Child Health and Human Development (NICHD), NIAID supports the Diabetes Prevention Trial-Type 1, a multi-site cooperative clinical trial on the prevention of insulin dependent diabetes mellitus (IDDM) in first degree relatives of patients with IDDM. This is the first large nationwide trial of an immunomodulatory agent for the prevention of an autoimmune disease. High-risk subjects are randomized to treatment with low-dose injections of insulin or no intervention. Intermediate risk subjects are randomized in a placebo-controlled, double-masked trial with oral insulin as the intervention. The trial is expected to run until 2002.

Systemic lupus erythematosus (SLE) is estimated to affect 131,000 Americans, with 90 percent being women of childbearing age. The disease often starts between the ages of 15 and 44. People of all races may get lupus; however, lupus is three times more common in African American women than in white

Table 1. Hispanic American Subgroups in the United States and Percentage with Diabetes.

Hispanic American population	Percent of total Hispanic population	Year of study	Percent with diabetes, age 20-44	Percent with diabetes, age 45-74
Mexican Americans	64.3	1982-84	3.8	23.9
Mexican Americans	64.3	1988-94	--	26.2
Central/South Americans	13.4	--	--	--
Puerto Ricans	10.6	1982-84	4.1	26.1
Cuban Americans	4.7	1982-84	2.4	15.8
Other Hispanic Groups	7.0	--	--	--
-- No data available				

Note: In this table, diabetes is defined using earlier guidelines by a medical history of diabetes or a diabetic oral glucose tolerance test (fasting glucose of 140 mg/dL or greater or 2-hour glucose of 200 mg/dL or greater).

women. As many as 1 in 250 young African American women will get the disease, which is responsible for 14,000 hospitalizations per year.

NIAID is presently funding a small epidemiological study to investigate the prevalence of SLE in women in Africa, the Caribbean, and African American women in the United States. The findings from this study may provide clues concerning the genetic and environmental factors important in the pathogenesis of this disease. NIAID also supports a demonstration and education project addressing the effects of educating patients with lupus, particularly African American patients, about the complications of their disease.

In 1999, NIAID awarded grants to establish four Autoimmunity Centers of Excellence: University of Colorado, Denver; Columbia University, New York; Brigham and Women's Hospital, Boston; and University of Pennsylvania, Philadelphia. These centers will support a cooperative research program of integrated basic, pre-clinical, and clinical research. These centers will build on the successful program projects in autoimmunity by incorporating a clinical component into a program of research that focuses on the understanding of the defect in self-tolerance seen in autoimmune disease. The centers will conduct single and multi-site cooperative clinical trials for new immunomodulatory interventions and studies of mechanisms of action of tolerance induction. The clinical component will allow the piloting of novel immune therapies for these diseases.

With the advent of new technology, researchers now have the tools to take a more mechanistic approach to the question of why women are more prone to developing autoimmune diseases. To stimulate more high-quality research in this area, NIAID organized a meeting on gender and autoimmunity, and issued a program announcement asking for research applications in this field. The National Institute of Neurological Disorders and Stroke (NINDS), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute of Dental and Craniofacial Research (NIDCR), NIH's Office of Research on Women's Health (ORWH), and NIDDK also supported the meeting and the program announcement titled *Gender in the Pathogenesis of Autoimmunity: Mechanisms and Role of Microbes in Autoimmune and Immune-Mediated Diseases*.

Transplantation

NIAID research in the field of transplantation encompasses a variety of basic and clinical research efforts focused on addressing the higher incidence rates of end-stage renal disease (ESRD) among minority populations. These efforts include testing new modalities of immunosuppression to prevent kidney graft rejection through a cooperative clinical trial; screening, characterizing, and acquiring reagents for histocompatibility testing of transplantation antigens for African Americans, Hispanic/Latino, and Native Americans; and supporting several transplantation program projects and investigator-initiated studies involving immunologic mechanisms and potential immunotherapies in the prevention of graft rejection.

Today, hemodialysis, peritoneal dialysis, and renal transplantation are lifesaving treatment modalities for patients with partial or complete renal failure. However, the rate of occurrence of ESRD, specifically in minorities, continues to increase by more than 8 percent per year with immunologic diseases being responsible for a significant number of new ESRD cases. The incidence of IDDM, which can lead to renal failure, has increased at an average rate of 13 percent per year for the last 5 years, while glomerulonephritis, a heterogeneous group of immunologic diseases that target the glomerulus (the filtering unit of the kidney), continues to be the third major cause of ESRD.

Nearly 19,000 kidney transplants are performed each year in the United States. Transplantation is clearly the treatment of choice for ESRD because 60 percent of dialysis patients die within 3 months to 5 years. Therefore, research supported by NIAID aims to develop improved, specific immunosuppressive agents as well as understand and develop strategies to induce donor-specific tolerance in the transplant recipient, which would allow discontinuation of nonspecific immunosuppression.

In 1995, a total of 19,136 solid organ transplants were performed in the United States: 10,891 kidneys; 3,922 livers; 2,361 hearts; 110 pancreata; 871 lungs; 67 heart-lung combinations; and 914 kidney-pancreas combinations.

In 1993, 217,479 Americans with ESRD required treatment with dialysis (180,127) or transplantation (11,021). Reimbursements for all treatment modalities for ESRD beneficiaries totaled $11.1 billion in 1994: $8.3 billion from Medicare and $1.8 billion from third-party payers. As a comparison, the average cost for all Medicare services from 1991 to 1993 was $36,700 per year at risk per patient. For all dialysis patients, total Medicare payments for the same period was $43,700 per year at risk, whereas for transplant patients it was $17,600 per year. In addition, the life expectancy of ESRD patients is one-fourth to one-fifth that of the general population in the United States.

There is a racial disparity in renal transplantation rates. Although African Americans represent 34.3 percent of those awaiting kidney transplantation, they receive only 24.8 percent of the cadaveric transplants and 14.3 percent of living donor transplants. Similarly, there are fewer transplants among Asians (3.7 percent cadaveric and 4 percent living donor) than would be expected from their representation on the waiting list (5.1 percent).

Re-transplantation currently accounts for 17 percent of all kidney transplants, 15 percent of all liver transplants, and 2 to 5 percent of all other organ transplants. The number of patients being re-enrolled on waiting lists has increased each year.

In 1994, approximately 12,000 patients received allogeneic bone marrow transplants. When successful, bone marrow transplantation is curative therapy for immunodeficiency diseases, hematologic malignancies, aplastic anemia, and certain metabolic disorders. An additional 5,000 patients are potential candidates for marrow transplantation.

In order to prevent both graft rejection and graft-versus-host disease (GVHD), it is important for donors and recipients to be human lymphocyte antigen (HLA) identical. Success rates vary among the different diseases treatable by bone marrow transplantation, but for low-risk patients, 2-year, disease-free survival following unrelated bone marrow transplantation is 40 percent and drops to 19 percent for high-risk patients.

The Cooperative Clinical Trial in Transplantation, a multi-center clinical trial of new therapies for prolonging kidney graft survival, has finished enrollment in its donor-specific blood transfusion trial. The program has been successful at recruiting minority patients. Preliminary analysis has shown that this therapy does show efficacy in prolonging kidney graft survival, but the extent of this enhancement is not known. Patients will be followed for 10 years to determine if this therapy has a positive effect on long-term graft survival.

In FY 1994, NIAID established the Cooperative Clinical Trial in Pediatric Transplantation at 35 medical centers to examine new treatments to prevent the rejection of transplanted kidneys in children. This ongoing cooperative research program examines the causes of lower patient and graft survival rates in children versus adults and the effects of immunosuppressive therapy on growth retardation.

NIAID continues to chair and coordinate the NIH Transplantation Research Coordinating Committee. This committee fosters interactions not only among the various NIH institutes, centers, and divisions, but also between NIH and other Federal agencies. This open communication has enhanced the efficacy of federally funded projects in transplantation and has facilitated access to the various scientific and medical expertise needed for the planning and execution of these projects.

In a statewide program, the Louisiana Organ Procurement Agency is carrying out an NIAID-supported research project that combines education for donor target populations and for the medical community to enhance donation. This multifaceted project involves: (1) identification of individuals willing to become donors through the establishment of a donor registry based on the statewide driver's license identification information system; (2) development of an intense hospital education program to increase awareness of the need for more donors; (3)

initiation of intensified public and professional education efforts that target specific groups, including African Americans, to increase awareness of the need for donors; and (4) the development, testing, and evaluation of a behavioral strategy to increase family consent based on a theoretical model of various stages of readiness for decision-making.

Beginning in FY 1997, NIAID provided support to the University of Washington for a 5-year demonstration and education research project to evaluate the effectiveness of a unique community-based outreach network in increasing organ donation among minority populations in Seattle and Tacoma, Washington. This project involves: (1) the development and distribution of educational materials in local neighborhoods and churches, using the services of VISTA (Volunteers in Service to America) participants recruited from targeted African American and Asian communities; (2) the production of an educational video for local communities and schools; (3) the dissemination of public service announcements at Department of Motor Vehicles offices; and (4) the development of a computerized database of community residents to record donation preferences, educational levels, and medical histories.

A second NIAID-supported University of Washington project is aimed at increasing donation among Alaskan Natives. Culturally sensitive educational materials and community health education programs are being developed on transplant options and living and cadaveric organ donation for this population, including an educational video featuring Alaskan Native transplant recipients and donor families; an attitudinal survey; and regional training for Native Corporation local health educators, community health aides, local school teachers, and regional hospital staff. A key feature of this approach is to provide the training necessary to enable Alaskan Natives to introduce to their communities the information necessary for informed decision-making.

Based on input from the scientific community and recommendations from expert panels, NIAID developed a Request for Proposals (RFP) titled *Collaborative Network for Clinical Research on Immune Tolerance*. This network will be a consortium of institutions and organizations that will develop a long-term scientific agenda to accelerate clinical studies in immune tolerance, and will conduct clinical trials and mechanistic studies of tolerogenic protocols in the area of kidney and islet cell transplantation. In the future, NIAID intends to expand the network to include clinical research on allergy, asthma, and autoimmune diseases. This RFP is available online at the following web site: http://www.niaid.nih.gov/publications/immune/rfp1.htm.

Microbiology and Infectious Diseases

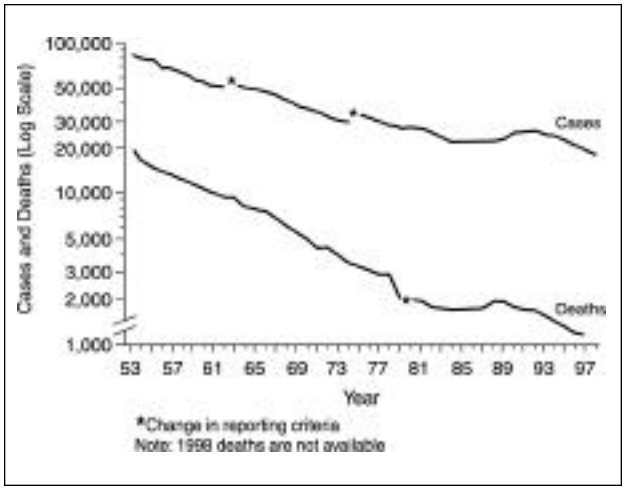
The microbiology and infectious diseases segment of the Institute's scientific agenda includes intramural and extramural research to control and prevent diseases caused by virtually every infectious agent. Institute support includes a wide spectrum of projects spanning basic biomedical research, such as studies of microbial physiology and antigenic structure, to applied research, including the development of diagnostic tests and clinical trials to evaluate potential drugs and vaccines. NIAID currently supports approximately 300 clinical studies and seeks to expand recruitment of minority populations into these studies.

One of the Institute's primary goals is to broaden the impact of vaccines in preventing disease. Since 1981, NIAID has supported a program for the accelerated development of new vaccines to direct the rapid advances in molecular biology, immunology, genetics, and epidemiology for the development and clinical testing of new vaccines.

Tuberculosis

A century ago, tuberculosis (TB) was a leading cause of death in the United States. Through the efforts of physicians, researchers, and public health officials, and especially improvements in living conditions and the introduction of effective drug therapy, the number of TB cases and deaths in the United States had declined steadily from the early 20th century until 1985 (see Figure 2).

Figure 2. Tuberculosis Cases and Deaths, United States, 1953-1998.



During the period of 1985 to 1992, new cases of TB in the United States unexpectedly increased 20 percent, from 22,201 to 26,673. Starting in 1993, however, there has been a steady decrease in the total number of new TB cases each year. In 1998, a total of 18,361 new cases of TB were reported to CDC from the 50 States and the District of Columbia, representing an 8 percent decrease from 1997 and continuing the downward trend first noted in 1993.

The continued downward trend is thought to reflect at least six factors:

- Improved laboratory methods for prompt identification of *Mycobacterium tuberculosis*;
- Broader use of drug susceptibility testing;
- Expanded use of preventive therapy in high-risk groups;
- Implementation of measures to limit transmission of *M. tuberculosis* in congregate settings including hospitals, homeless shelters, and HIV treatment facilities;
- Improved follow-up of diagnosed cases; and
- Increased Federal resources.

Despite this progress, 12 States reported no change or an increase in the number of TB cases between 1997 and 1998.

During 1998, approximately 75 percent of the active cases of TB were reported among racial and ethnic minorities. The disproportionate impact of TB among minorities is due largely to a combination of some of the problems related to urban poverty: overcrowded living conditions, HIV infection, and inadequate treatment and/or compliance with TB chemotherapy. Compared with 1997, the total number of reported cases of TB in the United States in 1998 decreased by an average of 7.5 percent in all racial and ethnic groups.

The link between HIV and TB is thought to be a significant factor in the spread of TB. In 1997, of the 8 million estimated new cases of active disease per year worldwide, 8 percent are coinfected with HIV. Tuberculosis is now the leading cause of death in HIV-infected persons, responsible for more than 50 percent of AIDS deaths in HIV endemic regions worldwide. Furthermore, TB remains more difficult to diagnose in HIV infected patients, making inadvertent transmission to both HIV-positive and -negative persons both more likely and more difficult to control.

The TB crisis is intensified by the emergence of disease caused by multi-drug resistant organisms. Infections caused by these organisms may result in an essentially incurable form of the disease, capable of spreading by casual contact. Multi-drug resistant TB represents a small percentage of total cases in the United States, but has been identified in 45 States and the District of Columbia. Drug-resistant strains are more difficult and vastly more expensive to treat. Unfortunately, patients with drug-resistant TB may remain infectious longer because of inadequate treatment.

In response to this urgent problem, NIAID dramatically increased funding for TB research during recent years, from approximately $3.5 million in 1991 to approximately $40 million in 1999. This increased funding has allowed the Institute to fund a number of initiatives and a markedly increased community of TB researchers. It enabled NIAID to

establish the Tuberculosis Research Unit (TBRU) in 1994 at Case Western Reserve University, and to recently recompete this contract-funded unit for an additional 7-year contract period. TBRU encompasses an international, multidisciplinary team of collaborators that has begun to address several important goals for the ultimate translation of TB basic research findings to the clinical arena.

TBRU-initiated studies are developing or evaluating a variety of potential new assays, markers, prevention strategies, and therapeutics, including the following: adjunctive immunotherapeutics, including *Mycobacterium vaccae (M. vaccae)* and intradermal IL-2; a new rifamycin derivative with a longer half-life than rifampin; auxotrophic vaccines; and a number of potential surrogate markers for disease progression, including development of an assay based on the measurement of antigen 85BmRNA. In addition, TBRU is conducting a household contact study of tuberculosis patients in Uganda to further understand disease transmission and to attempt to identify correlates of the protective human immune response. International collaborators and clinical trial sites in Uganda and Brazil, as well as U.S.-based collaborators and trial sites, make these studies possible.

NIAID supports investigator-initiated research and provides research materials and services to help TB researchers overcome significant technical obstacles. NIAID provides TB research reagents to qualified investigators throughout the world, enabling them to work with consistent, high quality reagents prepared from the highly contagious and technically demanding causative pathogen, *M. tuberculosis*. Screening potential anti-TB vaccine candidates in appropriate animal models is also supported by NIAID. More than 50 potential candidate vaccines have been screened, including recombinant Bacille Calmette-Guerin (BCG) strains expressing cytokines, auxotrophic BCG strains, *M. vaccae*, culture filtrate proteins, subunit vaccines, and nucleic acid-based vaccines.

NIAID contracts are screening for new drugs to treat tuberculosis. More than 43,000 compounds have been submitted from investigators worldwide for screening against *M. tuberculosis*. In addition, NIAID supports three academic groups that collaborate with pharmaceutical firms to stimulate discovery of new anti-TB drugs and provides contractual funding to facilitate translation of anti-TB discoveries into candidates for development and commercialization.

Internationally, NIAID is working to impact the global TB epidemic. Three International Collaborations in Infectious Disease Research (ICIDR) cooperative agreements were recently awarded to support collaborative TB research efforts between U.S. investigators and research groups from TB endemic countries. NIAID is cofunding, with NHLBI, an RFA to support development of improved animal models for TB, particularly in the areas of persistence and reactivation of disease because most cases of TB arise in persistently infected individuals (roughly 2 billion people, globally). In collaboration with the Fogarty International Center, NIAID is supporting seven new supplemental training awards to improve global health research and public health capacity for response to the TB epidemic.

TB vaccine development is a priority for NIAID because improved vaccines are crucial to the long-term control of TB worldwide. NIAID presented a *Blueprint for TB Vaccine Development* at the 1998 International Symposium for Tuberculosis Vaccine Development and Evaluation. The *TB Blueprint Report* outlines the specific steps needed to develop improved TB vaccines. A trans-DHHS Task Force, which includes representation from NIAID, will oversee implementation of the *TB Blueprint Report*.

Sexually Transmitted Diseases

Sexually transmitted diseases (STDs) are critical global and national health priorities because of the devastating impact on women and infants and the causal association with HIV infection. STDs often have severe sequelae such as infertility, tubal pregnancy, cervical cancer, fetal wastage, low birth weight, congenital or perinatal infection, and HIV infection. Recent studies indicate that the more prevalent nonulcerative STDs (chlamydia, gonorrhea, and trichomoniasis) as well as ulcerative diseases (genital herpes, syphilis, and chancroid)

increase the risk of HIV transmission by at least threefold to fivefold. Because of the lack of a functioning immune system, HIV infection can result in alteration of the natural history of some STDs (e.g., pelvic inflammatory disease and human papillomavirus infection).

The current STD epidemic in the United States disproportionately affects minorities. Both the incidence of STDs and their long-term, in some cases life-threatening, consequences are higher among nonwhites than they are among whites. For example, since the syphilis epidemic of the 1990s, syphilis rates declined in all regions of the United States. However, a closer look at the demographics reveals that since 1990, reported rates of syphilis have declined among all racial and ethnic groups except Native Americans and Alaskan Natives. Among the African American and Hispanic populations, the national rates are 2.6 cases per 100,000 population. While this is the lowest rate since the discovery of penicillin, it still exceeds the reported rate for Caucasians (0.5 cases per 100,000).

Moreover, although African American and Hispanic/Latina women comprise only 17 percent of the total female population of the United States, they represent a disproportionate share (33 percent) of the consultations for pelvic inflammatory disease (PID). PID is a disease of the upper reproductive tract that is primarily caused by sexually transmitted bacterial infections. Chronic complications include partial or complete tubal scarring. Among all populations, adolescents bear an enormous burden of disease. In 1998, 64 percent of the 14 million incident cases of STDs occurred in young people under age 24; more than 3 million cases occurred in teens.

In light of the spiraling acute and chronic morbidity of STDs, STD research is a high priority at NIAID. A systematic attack on STDs must emphasize the health effects of STDs in women and the interrelationships between STDs and HIV infection and include augmented efforts to:

- Develop effective behavioral interventions;
- Develop topical microbicides;
- Develop safe, effective vaccines;
- Develop rapid, inexpensive STD diagnostics;
- Prevent and control sequelae of gonorrhea and chlamydial infection in women such as PID and its complications (i.e., infertility, ectopic pregnancy, and chronic pelvic pain syndromes) and adverse outcomes of pregnancy;
- Elucidate the epidemiology, pathogenesis, and natural history of genital ulcer diseases, including STDs/HIV interactions;
- Delineate the pathogenesis, natural history, and management of human papillomavirus infection; and
- Develop a multidisciplinary research agenda on adolescents and STDs.

NIAID currently has several STD research activities underway to address these debilitating diseases. The Institute has intensified research efforts in syphilis especially in the development of new, improved biomedical tools to complement and sustain the CDC's Syphilis Elimination Program. This initiative includes:

- Developing a rapid, inexpensive test that does not require a blood sample. Current efforts are underway to transfer technology for a saliva-based test;
- Evaluating treatment for syphilis. The objective is to further characterize a single-dose, oral therapy for primary, secondary, and early syphilis; and
- Stimulating vaccine development efforts by using the newly sequenced genome of the causative bacterium, *Treponema pallidum*.

The Institute currently funds a program project called Research on the Molecular Immunology of Syphilis at the University of Washington. Investigators have used newly identified surface antigens (based on genome sequence) to vaccinate rab-

bits and have achieved partial protection in this model.

NIAID supports seven STD Cooperative Research Centers (CRCs), which provide a multidisciplinary approach to STD research by bringing together basic science, clinical/epidemiologic research, and behavioral intervention strategies for the prevention and control of STDs. In summer 1996, the Institute launched a pilot research program with second-year medical students from Howard University in Washington, D.C. This program provides the students with a 10-week research experience in STDs at the STD CRCs and has the long-term objective of encouraging young minority physicians to pursue careers in STD research. The program, currently in its fourth year, is now supported by a training grant awarded to Howard University in 1999.

NIAID supports six program projects in the development of topical microbicides at Emory University, Johns Hopkins University, Pennsylvania State University, University of Cincinnati, University of Pittsburgh, and University of California at Los Angeles. Topical microbicides are intravaginal preparations that would be bactericidal or virucidal and used by women to prevent sexually transmitted infections, with or without spermicidal activity. The ideal product would have physical characteristics that render the microbicide invisible and amenable to use without partner knowledge or consent.

NIAID has supported several clinical trials to evaluate the safety and efficacy of currently available spermicides for prevention of STD/HIV infection. Several others are planned or in progress; these include evaluation of new classes of topical microbicides, some of which may prevent infection without preventing pregnancy.

To address the increasing problem of STDs and adolescents, NIAID has awarded a STD CRC devoted to research in adolescent populations. In addition, four large clinical studies are in progress focusing on minority adolescent populations, including Emory University; University of California, San Francisco; University of Alabama, Birmingham; and Magee Women's Hospital. Two school-based studies measuring the impact of urine-based screening on the prevalence of chlamydial infection are also in progress. In collaboration with the Rockefeller Foundation, NIAID will publish a monograph on the state-of-knowledge and a multidisciplinary research agenda that includes biomedical epidemiological, social, and behavioral research needs in adolescents and STDs.

Emerging Infectious Diseases

In its 1992 report on emerging infections, the Institute of Medicine's Committee on Emerging Microbial Threats to Health indicated that the threat posed by disease-causing microbes may be expected to continue and even intensify in coming years. The report detailed those factors contributing to the emergence of new human pathogens. These include changes in demographics and human behavior, such as the sheer increase in the global population, its local density in urban settings, and its spread into previously uninhabited regions, as well as the magnitude and speed of international travel. Such factors may increase the likelihood of contact between infectious agent and host.

In response to this problem, NIAID participated in an interagency Working Group on Emerging and Reemerging Infectious Diseases, which was established under the Committee on International Science, Engineering, and Technology (CISET) of the National Science and Technology Council. In 1995, the *CISET Report on Emerging and Reemerging Infectious Diseases* was presented at a public forum chaired by the Undersecretary for Global Affairs at the State Department. The report made a number of recommendations for action by the Government, including working with other countries, the World Health Organization (WHO), and other international organizations to improve worldwide disease surveillance, reporting, and response, as well as strengthening the U.S. capacity to combat emerging diseases, including supporting an active community of epidemiologists, clinical investigators, laboratory scientists, health experts, and behavioral scientists.

In 1996, NIAID released its *Research Agenda for Emerging Infectious Diseases* to provide an integrated and proactive research strategy that will ensure pre-

paredness to address the health problems presented by emerging infectious diseases. Goals of this agenda include the following:

- Strengthening basic and applied research on the multiple hosts, pathogens, and environmental factors that influence disease emergence;

- Supporting the development of diagnostics, vaccines, and therapies necessary to detect and control infectious diseases; and

- Maintaining the national and international scientific expertise required to respond to future health threats.

Hantavirus

A hantavirus spread by rodents in the southwestern United States is thought to have emerged at least partially as a result of climatic conditions favorable for increases in rodent populations. The outbreak started in June 1993, with the observation of a disease cluster of unknown etiology associated with a highly fatal respiratory illness in the four-corner region of the Southwest. The disease was identified as hantavirus pulmonary syndrome (HPS). By October 1994, 91 cases were reported with illnesses meeting the surveillance case definition of HPS. Fifty-one percent of these patients died. Nearly 35 percent of the cases occurred in Native Americans.

NIAID made three awards in 1996 in response to an RFA titled *Hantavirus and Other Emerging Virus Threats*. These Emerging Viruses Research Groups (EVRGs) perform multidisciplinary, collaborative research on emerging viral diseases in general, with special emphasis on hantaviruses. Furthermore, EVRGs develop coordinated basic and applied research projects yielding new data that will enhance prediction, prevention, treatment, and control of emerging and reemerging viral diseases threatening the United States. They are located at the University of Texas Medical Branch at Galveston; Scripps Institute in La Jolla, California; and the University of New Mexico in Albuquerque. Two of the centers have been cofunded by the National Aeronautics and Space Administration to include pilot projects using geographic information satellite systems to analyze environmental factors influencing a disease.

NIAID's Collaborative Antiviral Study Group has initiated a clinical trial of ribavirin therapy for hantavirus pulmonary syndrome. The protocol committee includes investigators with expertise in severe respiratory infections and ribavirin, representatives from the Indian Health Service and the Navajo Nation, and appropriate staff from CDC, the U.S. Food and Drug Administration (FDA), and NIAID.

Hepatitis C

Ten years ago hepatitis C virus (HCV) was identified as a blood-borne pathogen that infects cells of the liver. Unfortunately, most people who are infected do not recover but go on to develop a lifelong chronic infection. Within 20 years of infection, about 20 percent develop severe scarring of the liver that significantly hampers and can stop the functioning of this vital organ, leading to death; another 4 percent develop liver cancer that is also fatal. CDC recently reported that 3.9 million Americans have evidence of infection, with three-fourths still active carriers of the virus. A peak of incidence was observed in the late 1980s with more than 200,000 cases per year. Although incidence has decreased, the long natural history leads CDC to predict a significant rise in illness due to HCV in roughly 15 years. At this point, HCV will actually cause more deaths in the United States than AIDS. Even now, HCV is the leading reason for liver transplants and beyond these costs, accounts for an additional $600 million in medical costs each year.

Various population-based surveys indicate that HCV impacts more heavily on minority populations in the United States. More than 3 percent of African Americans and more than 2 percent of Mexican Americans are infected compared to 1.5 percent of non-Hispanic whites. Examining sera from healthy young adults demonstrated that even 50 years ago, African Americans were more likely than Caucasians to be positive for antibodies to hepatitis C virus.

HCV is unlike HIV in that treatments can lead to long lasting clearance of virus. Treatments for HCV infection are limited to various interferon prepara-

tions and interferon in combination with ribavirin. They are not terribly effective, with their general effectiveness hovering around 10 percent for monotherapies and 30 percent for combined therapy. Unfortunately, even when matched for age and initial levels of HVC RNA in the serum, African American HCV patients, with similar disease characteristics as Hispanics, Asians, and whites, are much less apt to demonstrate end-of-treatment response (12 percent versus 33 percent) or sustained response (2 percent versus 5 percent) to interferon therapy. These differences are as yet unexplained.

The four Hepatitis C Cooperative Research Centers that were launched in 1996 are basic and clinical research units devoted to understanding the infection and disease processes. Two have as their primary focus minority populations. The first follows a large, inner city, injection drug-using cohort that is predominantly African American. The second cohort is Alaskan Natives. This research is examining natural history as well as persistence and pathogenesis from both the virus and host perspectives. Pilot projects associated with these centers have been instrumental in bringing new investigators and ideas into the field.

NIH sponsored a Consensus Development Conference on the Management of hepatitis C in 1997 (http://odp.od.nih.gov/consensus/cons/105/105_intro.htm) whose recommendations included evaluation of available therapies in minority patients and development of new therapies. With the help of outside experts, NIAID developed a *Framework for Progress for Hepatitis C*. This document defines the major basic and clinical research goals, questions, resources, and tools needed to achieve these research goals. This can be accessed at (http://www.niaid.nih.gov/dmid/hepcframe.htm).

NIAID also supports the Collaborative Antiviral Studies Group (CASG) that in 1996 authorized the inclusion of clinical trials in hepatitis C. An advantage of CASG is that it targets underserved populations as well as tests novel antivirals either alone or in combination with others. One of the first studies will evaluate an antibody for use in preventing recurrence of infection of the new liver when HCV-positive patients receive liver transplants. In FY 1999, NIAID funded more than $12.2 million in research on hepatitis C. NIAID has been trying to increase its research portfolio in hepatitis C and has initiated and participated in several efforts. These include studies on emerging diseases, enteric and hepatic infectious diseases, and prevention of recurrent disease after liver transplantation.

Childhood Diseases and Pneumonia

The health of infants and children is influenced greatly by a variety of socioeconomic factors and is generally considered to be a reliable indicator of the quality of health care services available and provided within a given community. Although the infant mortality rate often is used to gauge the health of infants within a specific socioeconomic group, child health is more difficult to assess precisely. Both are directly related to the quality of prenatal and postnatal care administered.

Between 1981 and 1988, a steady average of 3,000 cases of measles occurred each year. This rate was a reduction of more than 99 percent from the 400,000 to 700,000 annual cases reported before the introduction of a vaccine in 1963. However, a recent resurgence of measles has occurred in the United States. From 1989 to 1991, the number of measles cases rose dramatically to 55,165 with 11,000 hospitalizations and 130 deaths reported. Before this epidemic, there was a decline in the immunization levels of children under 2 years of age. Thus, the major cause of the reemergence of measles in the United States was the failure to vaccinate children at the appropriate age rather than failure of vaccine efficacy. This served as a wake-up call to the public health community to reassess the measles control strategy. Since then, a two-dose measles vaccine schedule has been recommended and widely implemented in the United States. This effort has significantly reduced endemic measles throughout the United States, with an estimated 301 cases reported to CDC in 1995, providing new hope for the elimination of measles.

Group B streptococcus (GBS) has been the single most frequent cause of life-threatening bacterial infection (pneumonia, septicemia, meningitis) during the first 2 months of life for the past 2 decades.

Transmission is from mother to child, either *in utero* or during birth. GBS can also cause serious illness in pregnant women, postpartum women, and adults with chronic medical conditions. In 1990, GBS infections caused an estimated 7,600 serious illnesses and 310 deaths among infants younger than 3 months of age in the United States. Infections among newborn infants (illness onset at less than 7 days of age) accounted for approximately 80 percent of these illnesses. During the past 10 years a decline in neonatal GBS disease has occurred, which reflects the impact of adopting colonization screening and antimicrobial prophylaxis strategies for the prevention of neonatal GBS disease by relevant professional and public health communities. The overall annual incidence of early-onset GBS disease in designated surveillance areas declined 24 percent, from 1.7 cases per 1000 live-born infants in 1993 to 1.3 per 1000 in 1995, and is estimated as less than 1 per 1000 in 1997. During the same period (1993-1995), the rates of late-onset neonatal disease (illness onset at age 7 to 90 days) and of GBS disease for adults remained stable. The incidence of GBS is higher among African Americans and Hispanics/Latinos than among whites.

Active immunization of women to passively protect their newborns has great potential for prevention of maternal and infant disease. Five types of GBS (Ia, Ib, II, III, and V) have been identified by the variations in the composition and structure of their capsular polysaccharide. Although all types are responsible for disease, type III is more frequently implicated. In the last 8 years, a concerted effort has been made to develop and clinically test polysaccharide-protein conjugate vaccines with enhanced immunogenicity.

NIAID also supports research on the development of new or improved vaccines against infectious agents that contribute significantly to childhood morbidity and mortality. Such infectious agents include respiratory syncytial virus, rotavirus, streptococci, influenza and parainfluenza viruses, measles and rubella viruses, *Bordetella pertussis*, and poliovirus. Research also is being supported on the development of vaccines to prevent the occurrence of congenital birth defects caused by cytomegalovirus, toxoplasma, syphilis, herpesviruses, gonorrhea, chlamydia, and other infectious agents.

Experience indicates that following the licensure of vaccines to prevent major childhood diseases, the incidence of those diseases decrease. However, in the mid to late 1980s, the United States experienced an epidemic in four major childhood diseases; namely, measles, mumps, rubella, and whooping cough.

Prior to immunization, pertussis (whooping cough) was widespread, with high morbidity and mortality in infants and young children. Since the 1940s, whole-cell pertussis vaccines, consisting of chemically inactivated preparations of killed *B. pertussis* cells, have been effective in providing immunity to infants. The administration of the whole-cell vaccine was, however, temporarily associated with a series of adverse events ranging from unpleasant to severe, which led to its decreased acceptance in many countries. As part of the National Childhood Injury Act directed by Congress and with support by the National Vaccine Program, NIAID was mandated to address scientifically and systematically issues surrounding the safety of the current whole-cell pertussis vaccine. In addition, the Institute supported studies in the development and clinical testing of acellular pertussis vaccines, which led to their licensure in 1997. Following the licensure of the acellular vaccines, acceptance by physicians and parents has increased dramatically with more than 90 percent of U.S. infants now receiving the primary series of DtaP immunizations.

Prior to licensure and use of effective *Haemophilus influenzae* type b (Hib) vaccines, an estimated 1 in 200 children developed invasive Hib disease before 5 years of age. Two-thirds of the disease occurred in young infants. From 1989 to 1997, the age-specific incidence of Hib disease among children younger than 5 years of age decreased 99 percent from 34 to 0.4 per 100,000. This coincided with increases in doses of Hib polysaccharide vaccine distributed in the United States. In 1997, 258 cases of invasive *Haemophilus* disease (1.3 per 100,000) in children younger than 5 years of age were reported compared with 280 cases reported in 1996 (1.5 per 100,000). Of the 258 cases in 1997, serotype data were report-

ed for 200 (78 percent) of the cases, and of those, 81 (41 percent) were type b, the only serotype of *H. influenzae* currently preventable by immunization. The total number of cases of invasive Hib disease in 1998 was 54. Although the average annual incidence of Hib invasive disease per 100,000 children aged less than 5 years was 0.5 among non-Hispanic whites, race and ethnicity data for Native Americans and Alaskan Natives continued to show a high incidence of 12.4 per 100,000 children.

NIAID continues to support research on the epidemiology of GBS disease, basic biology of GBS and group A streptococci, GBS vaccine research, and clinical trials of GBS conjugate vaccines through a 5-year multidisciplinary contract awarded in late 1997 to the Channing Laboratory at Brigham and Women's Hospital in Boston. In phase I and II safety and immunogenicity trials of types Ia, Ib, II, III, and V GBS conjugate vaccines, these vaccines were found to be safe and considerably more immunogenic than the polysaccharide vaccines. The antibodies induced are functional, and the response appears durable for at least 2 years.

NIAID sponsored the Good Manufacturing Practices (GMP) production of three clinical lots of GBS type III conjugate vaccine. These vaccines have been used in a number of phase I and II clinical trials and have been found to be safe and immunogenic.

The Institute is sponsoring, as part of the Maternal Immunization Program, phase I safety and immunogenicity trials at Baylor College of Medicine, utilizing a group B streptococcal type III polysaccharide-tetanus toxoid conjugate vaccine and an RSV purified protein vaccine in third trimester pregnant women. These vaccines have previously been shown to be safe and well tolerated in postpartum women and women of childbearing age.

NIAID strives to accelerate research in bacterial respiratory pathogen vaccine development and use. A major emphasis is the immunological response of infants, the elderly, and various high-risk groups, such as Native American infants. Current vaccine development and testing relate to pneumonia, meningitis, bacteremia, neonatal sepsis, and otitis media. All of these are associated with *Streptococcus pneumoniae*, GBS, and meningococcal disease.

An infant immunization efficacy trial with PRP-T, a Hib conjugate vaccine, conducted in The Gambia in West Africa, demonstrated that the vaccine was efficacious in preventing invasive disease in infants and pneumonia caused by Hib. This is the first demonstration of the impact of Hib conjugate vaccines on pneumonia prevention and has enormous ramifications for vaccine implementation in developing countries where *Haemophilus influenzae* type b is the second most frequent bacterial cause of childhood pneumonia.

As a prelude to an efficacy trial, NIAID is currently sponsoring a phase II safety and immunogenicity trial of a nine-valent pneumococcal conjugate vaccine in The Gambia, West Africa. The trial is designed to determine whether the coadministration of the pneumococcal conjugate vaccine with DPT/Hib (Tetramune) in the same syringe alters the incidence of side effects or reduces significantly the immunogenicity component of the mixtures as compared with administration of the vaccines in separate syringes. The phase II trial has enrolled 590 infants aged 2 to 4 months. Serology data are currently being collected and analyzed.

Acquired Immunodeficiency Syndrome

Since the emergence of AIDS in 1981 as a deadly global infectious disease, considerable progress has been made in understanding how HIV attacks the immune system to cause disease and how to intervene therapeutically. Researchers have developed new techniques to detect HIV in blood and tissue and have identified powerful new antiviral therapies to suppress the virus and delay disease progression and death. New therapeutic regimens using potent protease inhibitors, commonly referred to as highly active antiretroviral therapy or HAART, have greatly improved the quality of life of many HIV-infected people in the United States and have led to dramatic declines in AIDS-related deaths. Between 1996 and 1997, after protease inhibitors were first introduced, deaths due to AIDS in the United States declined by a dramatic 42 percent.

Transmission due to substance abuse continues to be a significant factor in contributing to the spread of HIV in minority communities. Through December 1998, among people with AIDS reported to CDC, 43 percent of African Americans and Hispanic/Latino adults reported injection drug use as a potential exposure to HIV, whereas only 18 percent of whites reported the same potential for exposure.

The toll of substance abuse in many minority communities carries over to the epidemic in women. A large proportion of women becomes infected during sex with an injection drug user. More than 80 percent of the HIV-infected women in this country are of African American or Hispanic ethnicity and most were infected through heterosexual sex. As a consequence, the majority of HIV-infected children in this country are African American or Hispanic/Latino.

One of the greatest challenges facing AIDS researchers today is the recruitment and retention of minority patients for clinical trials. People of minority background face unique social, economic, and medical problems in coping with the challenges attendant to HIV infection. As the epidemic expands in minority communities, inclusion of these patients in clinical trials is particularly urgent to ensure that the results of research are applicable to all populations impacted by the disease. An additional challenge is the recruitment of underrepresented minority investigators to AIDS and AIDS-related clinical and basic research disciplines.

NIAID supports a comprehensive portfolio of biomedical and behavioral research aimed at preventing and treating HIV disease in minority communities, training minority investigators, and fostering infrastructure development.

The Institute has taken strong steps to ensure minority participation in clinical trials, natural history studies, and in prevention studies to assure that enrollment is reflective of the national epidemic. In reaching out to these populations, the NIAID Division of Acquired Immunodeficiency Syndrome (DAIDS) works with communities to identify and overcome barriers to participation in clinical trials. This is accomplished by developing culturally sensitive education materials, and by providing additional resources (childcare, transportation) necessary for enhancing participation of all communities in DAIDS-sponsored trials.

NIAID directs a large national clinical trials program consisting of three groups: the Adult AIDS Clinical Trials Group (AACTG), the Terry Beirn Community Programs for Clinical Research on AIDS (CPCRA), and the Pediatric AIDS Clinical Trials Group (PACTG). Each of these groups strives to ensure that a sufficient proportion of minority subjects are enrolled into clinical trials so that the results of the research may be generalizable to the affected HIV population at large. Of the 12,438 patients who were on studies in the Pediatric or Adult AIDS Clinical Trials Groups during FY 99, 38.4 percent were African American, 19.3 percent were Hispanic, 1.1 percent were Asian/Pacific Islander, and .6 percent were Native American. Of the 2,755 patients who were on CPCRA studies during FY 99, 39.6 percent were African American, 12.3 percent were Hispanic, .5 were percent Asian/Pacific Islander, and .5 percent were Native American.

NIAID's epidemiologic research explores the clinical course and factors contributing to transmission of HIV infection in a variety of populations. Groups of inner-city women and their children are the focus of the Women and Infants Transmission Study (WITS/WITSII). Likewise, the Women's Interagency HIV Study (WIHS), which explores the clinical course of HIV infection in women, targets minority women.

The Multicenter AIDS Cohort Study (MACS) is a prospective, longitudinal study of HIV disease in homosexual and bisexual men. This cohort has been followed for more than 15 years and is a valuable resource for information about the changing epidemic in the United States. In a second recruitment effort for MACS, minority populations were specifically targeted. Both MACS and WITS are studying access to medical care among people of minority background. The enrollment of individuals from minority communities in DAIDS-support-

ed epidemiology cohorts was 15 percent in MACS, 80 percent in WIHS, and 86 percent in WITS.

Vaccine Development

In the clinical component of vaccine research, NIAID directs the AIDS Vaccine Evaluation Units (AVEUs). AVEUs are making an increased effort to enroll minorities in phase I and phase II clinical trials of candidate HIV vaccines. The clinical research effort for evaluating vaccines and other modalities to prevent HIV infection or disease is currently centered in two large, multi-center organizations—the AIDS Vaccine Evaluation Group (AVEG) and the HIV Network for Prevention Trials (HIVNET). To date, more than 3,000 volunteers have participated in 52 clinical vaccine trials (50 phase I and 2 phase II trials).

AVEG focuses on early safety and immunogenicity trials, and correlative laboratory studies of candidate preventive vaccines. It carries out these phase I and phase II vaccine studies in a multi-center network of domestic U.S. sites. HIVNET has a broader agenda that includes trials of vaccines, topical microbicides, STD treatment, behavioral interventions, and approaches to prevent mother-to-infant transmission. It focuses primarily on efficacy trials (although it also carries out some phase I and II studies) in an international multi-center network. Scientific collaborations with scientists in industry and academia, and NIAID staff constitute other key components of the program.

The Vaccine Preparedness Study (VPS) is evaluating strategies for conducting future HIV vaccines and other preventive measures in populations at greater risk for contracting HIV in the United States. Study questions include what motivates people to enroll in HIV prevention trials and what prevents people who may be interested from enrolling. VPS, which was completed in January 1998, enrolled 4,892 participants from three groups at high risk for HIV: injection drug users, men who have anal intercourse (receptive or insertive) with other men, and women at high risk for HIV infection through heterosexual contact. In August 1997, an expansion of VPS was launched with the recruitment of new groups of injection drug users at HIVNET sites in Philadelphia and New York City. The expansion continued in February 1998 with the recruitment of participants from all three high-risk groups at five preexisting and three new HIVNET sites in Baltimore, Los Angeles, and the Bronx. These new sites enrolled primarily minorities. For the HIVNET Vaccine Preparedness Study, 40 percent of the enrollees were minority.

Prevention

The success of HIV prevention studies requires researchers and members of communities at risk for HIV infection to build trust by engaging in open, ongoing discussion. Establishing trust is critical since public confidence in the safety and integrity of medical research can be undercut by the legacy of previous research abuses, such as the Tuskegee Syphilis Study. Preparing and educating the community about HIV vaccine trials has been an important part of outreach for both HIVNET and AVEG. Community educators at each HIVNET site are helping community members to understand the science of HIV/AIDS and vaccines, as well as research methods and clinical trial processes, and they are responding to the educational needs of the community. These discussions include candid conversations about fears and concerns related to Government-sponsored research.

Both AVEG and HIVNET are currently undergoing a redesign and recompetition. These programs will evolve into the HIV Vaccine Trials Network and the HIV Prevention Trials Network. The HIV Vaccine Trials Network will conduct safety, immunogenicity, and laboratory-based studies of promising candidate HIV vaccines, including phase III studies.

The first NIAID-supported AIDS vaccine trial in Africa was initiated in Uganda in February 1999. This small phase I study, which is designed to evaluate Pasteur Merieux Connaught's (PMC) candidate vaccine ALVAC vCP205, will help determine if it is necessary to tailor-make vaccines for different parts of the world. ALVAC vCP205 is made up of a weakened canarypox virus that has been genetically altered to contain selected HIV genes: the *env* gene, the *gag* gene and a portion of the *pol* gene. The genes in the vaccine come from clade B viruses, the

predominant subtype of HIV found in the United States and Europe; however, the researchers will look for immune responses to clades A and D, as well as clade B viruses, because the former two subtypes cause most HIV infections in Uganda.

Another international vaccine trial is scheduled to begin in early 2000 in Brazil, Haiti, and Trinidad (HIVNET 026) to evaluate PMC's canarypox vCP1452 alone and in combination with a recombinant gp120 vaccine from Vaxgen. Each country will enroll 40 participants in this multi-center phase II trial.

Non-Vaccine Prevention Research

Since an HIV vaccine may only be partially effective, successful prevention strategies will likely require a combination of interventions. Also, since it is expected to take several more years to develop an effective vaccine, it is important to develop other promising interventions as rapidly as possible. Other strategies being pursued include topical microbicides, treatment of sexually transmitted diseases, which are cofactors for transmission, prophylaxis with antiviral drugs to prevent mother-to-child transmission, and behavioral risk reduction strategies for individuals and communities.

International studies to evaluate such non-vaccine interventions are currently underway in more than 20 developing countries. For example, HIVNET recently completed a behavioral intervention study (HIVNET 011) in Harare, Zimbabwe and found that peer education to promote condom use and safer sex practices among factory workers was a sustainable and cost-effective HIV prevention strategy. A prospective cohort study (HIVNET 021), which began in November 1999, is evaluating the effect of hormonal contraceptive use on the risk of HIV acquisition. The study, which is cosponsored by NICHD, will enroll 6,360 women from HIVNET sites in Zimbabwe, Uganda, and Thailand. Condom use and the incidence of STDs and HIV in the southern Philippines are also being evaluated by a group of NIAID-funded researchers to determine the effect of community-based education efforts.

Several international studies of topical microbicides, which are chemical barriers that can be used to inactivate HIV and other sexually transmitted diseases (STDs), are also underway. A topical microbicide would provide a reliable, female-controlled method for preventing HIV and, ideally, would be invisible, non-irritating, and inexpensive. Over the past year, more than 300 compounds have been tested for their ability to block HIV transmission from infected T cells to cultures of cells lining the human cervix and a number of promising topical microbicide candidates are in various stages of testing. An acid-buffering gel, BufferGel, that helps maintain the normal acidic environment of the vagina to disrupt the transmission of acid-sensitive STD pathogens, such as HIV, has been tested first in the United States and then in India, Thailand, Zimbabwe, and Malawi. It was found to be nontoxic and well tolerated. A phase III trial of N9 film in Cameroon was found to have no effect on transmission of HIV, gonorrhea, or chlamydia infections when provided as part of an overall HIV/STD prevention program. A separate phase III trial of a higher dose N9 gel (N9 Conceptrol) recently opened in Zimbabwe and Malawi. Safety studies of Pro 2000 have also been initiated in the United States, and will be followed by a companion trial in Durban and Johanessberg, South Africa. Plans are also underway to begin a trial of a caregeenan-based topical microbicide that blocks adherence of HIV to host cells in early 2000 in Capetown, South Africa.

The HIV Prevention Trials Network, a new initiative that will be funded in 2000, will continue to pursue these and other prevention strategies both domestically and internationally.

Mother-To-Infant Transmission

In early 1994, a long-course zidovudine regimen (AZT) used in the AIDS Clinical Trials Group study 076 was shown to be extremely effective at preventing perinatal transmission. Although it is now the standard of care for HIV-infected women in the United States, it is too expensive and impractical for widespread use in developing countries, where many women do not receive prenatal care. Shorter courses of AZT that are effective in reducing mother-to-infant transmission of HIV are still too expensive for

widespread use. With the goal of finding a simpler and less costly regimen suitable for global use, HIVNET evaluated the efficacy, safety, and tolerance of nevirapine (NVP) for reducing the risk of transmission of HIV from pregnant women to their infants. The study, which was conducted in Uganda, found that a single oral dose of nevirapine to an HIV-infected woman in labor and another to her baby within 3 days of birth reduced the transmission rate by half compared to a similar short course of AZT. This regimen, which costs approximately $4, could constitute a significant breakthrough for the developing world since this regimen could easily be implemented on a large scale.

Training Activities

The Centers for AIDS Research (CFARs) support a multidisciplinary environment that promotes basic, clinical, behavioral, and translational research in the prevention, detection, and treatment of HIV infection and AIDS. Some of the means by which CFARs accomplish this mission are by (1) fostering scientific communication; (2) sponsoring training and education; and (3) promoting community outreach. NIAID accomplishes these goals in part by promoting the development of minority scientists in AIDS research and addressing problems in enrollment and retention of women and minority groups in AIDS clinical trials.

Several CFARs have a significant commitment to minority investigators and minority communities. An example of this is the University of Washington (UW) CFAR, which provides research training opportunities to minority investigators, and has provided such assistance to 20 percent of students enrolled in the UW Minority International Research Training Program. It has also established an institutional and intellectual linkage between the AIDS Research Program at the University of Hawaii at Manoa (UHM) by directly supporting collaborative studies between CFAR investigators at UW and minority investigators at UHM. This collaborative effort permits UHM investigators to use core facilities at UW and to collaborate with investigators, thereby maximizing their productivity in order to be competitive for independent NIH funding.

NIAID Outreach Activities

NIAID outreach activities disseminate health-related materials and information and research results to minority communities as well as to the health professionals that serve them. These activities include producing and disseminating print and audiovisual materials, exhibiting at professional and community meetings, sponsoring workshops and conferences for community health care providers and the public, and supporting demonstration and education research projects.

NIAID produces materials on topics ranging from allergic and immunologic diseases to AIDS and other sexually transmitted diseases. These materials are distributed worldwide in response to more than 25,000 inquiries to the Institute each year. In addition, hundreds of thousands more download or request materials from the following NIAID web site: http://www.niaid.nih.gov.

Sexually transmitted diseases (STDs), such as pelvic inflammatory disease (PID) and syphilis, affect a disproportionate number of minorities. NIAID recently updated its nine fact sheets on STDs other than HIV/AIDS, which include PID and syphilis as well as genital herpes, vaginitis, and chlamydial infection. The STD fact sheets are the most requested materials on the NIAID web site.

NIAID is developing an AIDS vaccine communication campaign to increase awareness of AIDS vaccine research before the initiation of an efficacy study. Part of this campaign will include developing messages that will promote and enhance the participation of high-risk communities, including minorities, in NIAID-sponsored vaccine trials.

In 1999, the Institute published easy-to-read booklets in English and Spanish about tuberculosis. The booklets, *Learn About Tuberculosis* and *Learn About Tuberculosis Infection*, fill a critical need for patient information about an infectious disease that has a high incidence in many urban minority communities.

Also in 1999, NIAID published the booklet, *Understanding Autoimmune Diseases*. Autoimmune diseases, such as systemic lupus erythematosus (SLE), have a more detrimental effect on the health of African American women than any other group. This booklet gives descriptions of and general information on diagnosis and treatment of the most common autoimmune diseases such as type 1 diabetes and rheumatoid arthritis as well as SLE. It also contains a comprehensive list of resources for patients, their families, and their physicians.

NIAID continues to distribute its *How to Help Yourself/Ayudate* series of eight booklets on HIV/AIDS in English and Spanish to inner-city clinics, community health centers, and community-based organizations serving minority populations, as well as to correctional institutions. The booklets are also distributed by the CDC's National Prevention Information Network. NIAID plans to update these popular, easy-to-read booklets in the near future.

The Institute helps support a new NIH Spanish-language newsletter, *El Pulso de la Salud: Información de los Institutos Nacionales de la Salud*, which is distributed nationwide. NIAID serves on the NIH committee that publishes the newsletter and contributed articles on HIV/AIDS and sexually transmitted diseases in its first two editions.

NIAID Spanish-language materials are also on the NIH Hispanic Communication Initiative web site: http://www.nih.gov/welcome/hispanic/index.html.

During 1998 and 1999, NIAID staff distributed materials about allergic, immunologic, and infectious diseases and NIAID research and training programs to attendees at meetings sponsored by the National Medical Association, Society for Advancement of Chicanos and Native Americans in Science, the Hispanic Medical Association, the Student National Medical Association, the National Association for the Advancement of Colored People, the Society of Mexican American Engineers and Scientists, and the National Conference on Blacks in Higher Education, among others.

In response to requests from health professionals, NIAID distributed hundreds of copies of *A Guide for Helping Children with Asthma*. This guide was developed by the NIAID-funded National Cooperative Inner-City Asthma Study.

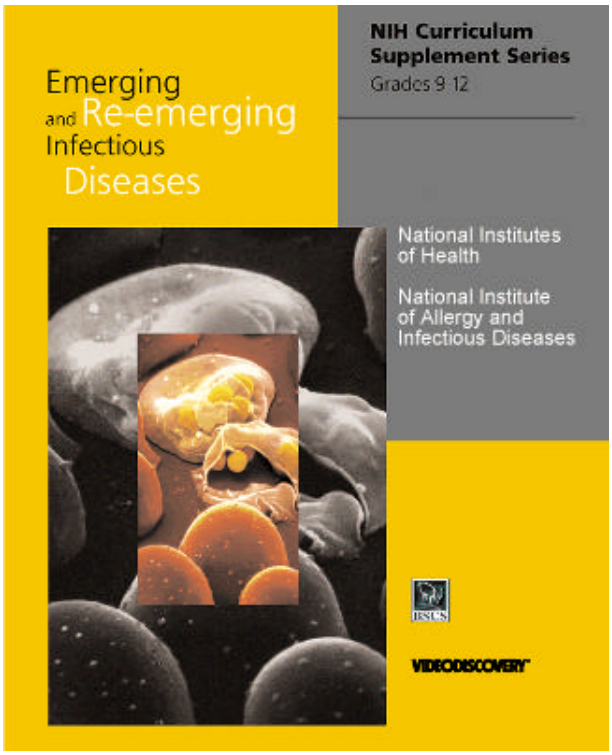
During the past 10 years, NIAID has worked with the National Asthma Education and Prevention Program in conjunction with NHLBI to foster the following goals:

- Raise awareness among patients, health professionals, and the public that asthma is a serious chronic disease;
- Ensure recognition of symptoms by patients, their families, and the public;
- Encourage appropriate diagnosis by health professionals; and
- Obtain effective control by encouraging a partnership among patients, physicians, and other health professionals through modern treatment and education programs.

In October 1999, NIH launched a major Curriculum Supplement Series for kindergarten through 12th grade at the National Convention of the National Association of Biology Teachers in Ft. Worth, TX. NIAID will be among the first three institutes to be in the first round of the nine-part series. The series will be distributed to teachers around the Nation free of charge by NIH to improve science literacy and to foster students' interest in science. The curricula contain new information about medical discoveries being made at NIH and their effects on public health.

The first three supplements are designed for use in senior high school classrooms. Each comes with an interactive CD-ROM. The NIAID curriculum is titled *Emerging and Re-Emerging Infectious Diseases*. This curriculum, in addition to *Cell Biology and Cancer* from NCI and *Human Genetic Variation* from the National Human Genome Research Institute (NHGRI), are among the first educational resources to be aligned with the National Science Education Standards released by the National

Academy of Sciences. The curricula can be requested from the Office of Science Education at http://science-education.nih.gov/supplements.



II. Minority Researchers' Training and Enhancement Programs

NIH-Wide Programs

Minority Biomedical Research Support Program

NIH strives to increase the number of minority researchers in the field of biomedical research. One of the largest programs at NIH that seeks to achieve this goal is the Minority Biomedical Research Support Program (MBRS). MBRS awards grants to educational institutions with substantial minority enrollments for the purpose of supporting research by faculty members; strengthening the institutions' biomedical research capabilities; and increasing the interest, skills, and competitiveness of students and faculty in pursuit of biomedical research careers. NIH provides funds to the National Institute of General Medicine (NIGM), who administers this program, for initiatives included in NIGM's research agenda. MBRS information is available online at http://grants.nih.gov/grants/guide/pa-files/PAR-99-152.html.

MBRS awards are made to 2- or 4-year colleges, universities, and health professional schools with enrollments that are comprised of at least 50 percent minority student populations. These populations have been determined by the grantee institution to be underrepresented in biomedical or behavioral research. Historically, individuals who have been found to be underrepresented in biomedical or behavioral research include, but are not limited to, African Americans, Hispanic Americans, Native Americans (including Alaskan Natives), and natives of the U.S. Pacific Islands. In some cases, awards are made to institutions that have demonstrated a commitment to the encouragement and assistance of minority students and faculty, although the minority student population at these institutions is less than 50 percent.

The MBRS Program has evolved into three major segments: Support of Continuous Research Excellence (SCORE), Research Initiative for Scientific Enhancement (RISE), and Initiative for Minority Student Development (IMSD). In FY 1999, NIAID supported five SCORE awards in the amount of $614,796 and provided an additional $357,158 for the student development portion of the RISE Program at Meharry Medical College.

The SCORE Program was designed to develop biomedical research faculty at minority-serving institutions who are committed to improving competitive research programs and increasing the number of underrepresented minorities professionally engaged in biomedical research. This is achieved by providing financial assistance to competitive, developing research programs in all areas of biomedical and behavioral research at institutions with significant underrepresented minority student enrollments. The program supports faculty-initiated, scientifically meritorious research programs including pilot research projects. The application must also include specific goals and measurable objectives against which they will be evaluated when they recompete for continued funding. Support for faculty participating in pilot research projects is preparatory to seeking more substantial funding from other NIH research grant programs such as the Academic Research Enhancement Awards and independent researcher project grants (R01).

The SCORE Program includes such allowable costs as faculty salaries, salaries for technicians, limited administrative support, consultant fees, equipment, research supplies, scientific seminar series, travel, and support for evaluation activities. Funds are also available for alterations and renovations to the institutions' facilities when deemed necessary to carry out the proposed research. Applicants may request support for up to 20 research projects and up to 8 pilot research projects per program. An institution is limited to one active SCORE award and may not be currently receiving support from the IMSD Program. SCORE Program information is available at the following web site:

http://grants.nih.gov/grants/guide/pa-files/PAR-99-152.html.

The RISE Program seeks to enhance the research environment at minority-serving institutions. The overall goal is to increase the interest, skills, and competitiveness of students and faculty in pursuit of biomedical research careers. The program offers support for faculty and student development activities, which can include on- or off-campus workshops, specialty courses, travel to scientific meetings, and research experiences at on- or off-campus laboratories. Support is available for evaluation activities, as well.

The RISE Program also offers support for institutional development, which includes limited funds for equipment purchases, the development of research courses, and the renovation or remodeling of existing facilities to provide space for an investigator to carry out developmental activities. An institution may hold only one active RISE award and may not be currently receiving support from the IMSD Program. As in the SCORE Program, the institutions are expected to set specific goals and measurable objectives against which they will be evaluated when they recompete for continued funding. Information about the RISE Program is available online at http://grants.nih.gov/grants/guide/pa-files/PAR-99-151.html.

The goal of the Initiative for Minority Student Development (IMSD) Program is to encourage the development and/or expansion of innovative programs to improve the academic and research competitiveness of underrepresented minority students at the undergraduate, graduate, or postdoctoral levels and to facilitate their progress toward careers in biomedical research.

These awards are open to domestic, private, and public educational institutions that are involved in biomedical research and training. The institutions are required to identify the student participants to be supported. These students must be majoring in the sciences relevant to biomedical research or be in training for a research career in medicine, dentistry, or veterinary medicine. The total requested project period for these awards may not exceed 4 years and are renewable. Allowable costs include, but are not limited to, graduate student tuition remission; supplies; equipment; travel; other expenses; and salary, wages, and fringe benefits for students and faculty.

Minority Access to Research Careers

The Minority Access to Research Careers (MARC) Undergraduate Student Training in Academic Research (U*STAR) Awards provide support for students who are members of minority groups that are underrepresented in the biomedical sciences to improve their preparation for graduate training in biomedical research. The program can also support efforts to strengthen the faculty, science course curricula, and biomedical research training programs and infrastructure at institutions with significant minority student enrollments. Additional information about this program is available online at http://grants.nih.gov/grants/guide/pa-files/PAR-99-150.html.

Awards are made to colleges and universities that offer the baccalaureate degree. The institutions are required to select the trainees to be supported. Trainees must be honors students majoring in the sciences who have an expressed interest in biomedical research careers and who intend to pursue postgraduate education leading to the Ph.D., M.D./Ph.D., or other professional degree/Ph.D. combinations. The period of appointment to the MARC U*STAR Program is 2 years at the junior or senior level.

Each institution is encouraged to design a program that emphasizes its environment, mission, and strengths and to set specific objectives and measurable goals against which the program will be evaluated when it recompetes for continued funding. Academic institutions that are not research-intensive may establish linkages with institutions that are research-intensive. Although variation among programs is expected, all programs should provide trainees with a summer research experience outside the home institution and with research opportunities during the academic year at the home institution or at another institution to which the U*STAR Program has established linkages. In addition to annual student stipends of $9,492 (FY 1999), funds

may be requested for tuition and fees for trainees, limited travel for trainees and faculty, and program evaluation activities.

The second rung of the U*STAR Program is the MARC Predoctoral Fellowships. These fellowships are for students who are graduates of the U*STAR Program. It is designed to provide outstanding U*STAR students with up to 5 years of support for research training leading to the Ph.D., M.D./Ph.D., or other combined professional degree/Ph.D. in the biomedical or behavioral sciences, including mathematics. Support is not available for individuals enrolled in medical or other professional degree schools unless they are enrolled in a combined professional degree/Ph.D. program in the biomedical or behavioral sciences.

The intent of the MARC Predoctoral Fellowship Program is to encourage students from minority groups underrepresented in the biomedical and behavioral sciences to seek graduate degrees. This furthers the NIH goal of increasing the number of underrepresented minority scientists who are competitively trained to pursue careers in biomedical or behavioral research. It is expected that training will be conducted in graduate degree programs of the highest quality. For more details on these fellowships, visit http://grants.nih.gov/grants/guide/pa-files/PAR-99-142.html.

The fellowship award, made under the auspices of the National Research Service Awards, provides an annual stipend of $14,688, a tuition and fee allowance in accordance with NIH policy, and an annual institutional allowance of $2,000, which may be used for travel to scientific meetings and for laboratory and other training expenses.

MARC Faculty Predoctoral Fellowships are awarded to faculty members of colleges or universities with significant minority enrollments. Awards provide an opportunity for eligible faculty who lack the Ph.D. degree (or equivalent) to obtain the research doctorate. Applicants must be full-time, permanent faculty in a biomedically-related science or mathematics program, and must have been at the minority institution for at least 3 years at the time of application. Candidates must be enrolled in or have been accepted into a Ph.D. or combined M.D./Ph.D. training program in the biomedical or behavioral sciences. The applicant must intend to return to the minority institution at the end of the training period. Additional information on this fellowship program for faculty is available at the following web site: http://grants.nih.gov/grants/guide/1994/94.02.18/pa-marc-faculty-rese010.html.

The award provides a stipend generally equal to the applicant's annual salary but may not exceed the stipend of a level 1 postdoctoral fellow ($27,720, FY 1999). The applicant may also request tuition and fees as determined by the training institution as well as an allowance of $2,000 per year for training-related costs. A maximum of 5 years of support is available.

MARC Faculty Senior Fellowships are awarded to eligible faculty at minority institutions to provide them the opportunity to update their research skills or move into new areas of research through a year-long period of intensive research in a state-of-the-art research environment. An applicant must be a full-time faculty member in a biomedically-related science or mathematics program for at least 3 years at the time of submission of the application. Moreover, the candidate must have received a Ph.D. or equivalent degree at least 7 years before the date of application. The candidate must intend to return to the minority institution at the end of the training period. The applicant may request no less than 1 academic year (9 months) and no more than 2 years of support. Additional information is available online: http://grants.nih.gov/grants/guide/1994/94.02.18/pa-marc-faculty-rese010.html.

The award includes a stipend generally equal to the applicant's salary but may not exceed the stipend of a level 7 postdoctoral fellow ($41,268, FY 1999). Awards made for less than 12 months will have funding prorated by the length of the award. The applicant may also request an institutional allowance of $3,000 per year to be used for expenses directly related to the training.

The Visiting Scientist Program provides support for periods of 3 to 12 months to outstanding

scientist/teachers who serve as visiting scientists at eligible minority institutions. The intent of the program is to strengthen research and teaching in the biomedical sciences for the benefit of the students and faculty at these institutions by drawing on the special talents of scientists from other primarily majority institutions. Awards are determined on an individual basis.

Research Supplements for Underrepresented Minorities Program

In 1989, NIH launched an initiative to provide funding for underrepresented minorities in biomedical research. The purpose of the Research Supplements for Underrepresented Minorities (RSUM) Program is to increase the number of underrepresented minorities in biomedical research through the use of supplements to research project grants currently being funded by NIH institutes and centers. Investigators in any institution with an existing grant may apply for supplemental funds to support a minority high school, college, postgraduate, postdoctoral, or junior faculty researcher to work in an area closely allied to the funded research. The length of the award may be tied to the length of the parent grant but is limited to a total award period not to exceed 4 years.

Under the RSUM Program guidelines, underrepresented minorities are defined as African American, Hispanic/Latino, Native American, Alaskan Native, Asian, or Pacific Islander. The thrust is to increase the total number of these minorities in biomedical research at every level of career development. Funds are provided for salary, tuition, fees, expendable supplies, travel, and other incidentals. The total yearly direct costs are not to exceed $50,000, of which up to $40,000 may be used for salary and benefits. Salary stipends are dependent on the level of experience and are consistent with the salary scales provided to investigators at the same level of experience in the grantee institution.

In FY 1999, NIAID funded 67 applications for more than $4.7 million. Awardees included minority investigators at the junior faculty, postdoctoral, predoctoral, undergraduate, and high school levels. The RSUM Program promises to be a continued success in increasing the total number of underrepresented minorities in biomedical research in areas of science relevant to NIAID's mission.

Research Centers in Minority Institutions

The Research Centers in Minority Institutions (RCMI) Program is designed to expand the national capability for research in the health sciences by assisting, through grant support, predominantly minority health professional schools and graduate institutions that offer a doctorate in the health professions or health-related sciences. The program assists these institutions in strengthening and augmenting their human and physical resources for the conduct of biomedical or behavioral research. The program also fosters faculty expansion and enrichment, physical facility improvement, and other research-related activities, including laboratory renovation and equipment replacement, that will assist such institutions to become more competitive in seeking funding for biomedical or behavioral research. To qualify as an RCMI, the institution must have more than 50 percent minority student enrollment and must be chartered to award a M.D., D.V.M., D.D.S., or Ph.D. degree in the health sciences. Currently, 19 institutions are participating in the RCMI Program.

The AIDS Infrastructure for the RCMI Program seeks to expand physical facilities and faculty competence in virology, immunology, molecular biology, and the neurosciences so that minority institutions may join mainstream AIDS research. These institutions are located in communities in which the AIDS epidemic has hit the hardest; therefore, they are uniquely suited to treat and recruit patients in clinical trials. Nine minority medical schools are eligible under the AIDS Infrastructure initiative: Howard University, Meharry Medical College, Morehouse School of Medicine, University of Puerto Rico, Universidad Central del Caribe, Ponce School of Medicine, Charles R. Drew School of Medicine and Science, University of Hawaii, and City University of New York.

NIAID actively participates in cofunding the AIDS Infrastructure initiative of the RCMI Program, which is administered by the National Center for

Research Resources (NCRR). In FY 1999, NIAID funded nearly $2.7 million to support RCMI projects in such diverse areas as clinical research, molecular vaccine development and drug development, opportunistic infections, and immunologic research.

In FY 1996, NIAID, the National Institute of Mental Health (NIMH), and the Office of Research on Minority Health supported an initiative to bring together NIAID's 12 Centers for AIDS Research (CFAR) investigators and match them with RCMI investigators to form collaborative pairs. Through these collaborative pairs, CFAR investigators facilitated access to CFAR-sponsored resources, such as state-of-the-art laboratories, emerging technologies, and interaction among AIDS investigators. The overriding goal of the initiative was to develop a level of expertise that will increase the possibility of a successful competition for funding. Eleven projects at seven schools, a total of 22 investigators, were selected. Schools participating in the collaboration program are Charles R. Drew University, City University of New York, Meharry School of Medicine, Morehouse School of Medicine, Texas Southern University, Tuskegee University, and University of Puerto Rico.

NIAID's belief that these initial scientific collaborations between majority and minority institutions would lead to future collaborations has been well founded. As a result of this pilot project, CFAR/RCMI investigator collaborations are very much a part of our AIDS program.

NIAID Programs

In FY 2000, NIAID plans to make available an electronic submission process for two of its minority programs. In early 2000, it will support an electronic PHS 698 Grant Application form for the submission of applications to its Research Supplement to Underrepresented Minority (RSUM) researchers. Following shortly thereafter in the summer of 2000, its highly successful Introduction to Biomedical Research Program (IBRP) will also have its application form placed on the NIAID web site (http://www.niaid.nih.gov). Both are being developed in response to numerous requests from interested individuals for an online application.

Office of Special Emphasis

In 1996, the Director, NIAID, established the Office of Special Emphasis within the Division of Intramural Research (DIR). Dr. Richard Asofsky was named as the Assistant Director to the Director, DIR, and head of the newly formed office. The Office is responsible for the design of training programs for NIAID intramural staff, outreach to and recruitment of underrepresented minorities, and support for the conduct of Institute programs such as the Introduction to Biomedical Research Program (IBRP), NIH Summer Internship Programs, and the recruitment of minority fellows.

Office of Special Populations and Research Training

In January 1998, the Director of NIAID created the Office of Special Populations and Research Training (OSPRT). OSPRT combines the functions formerly housed in the Office of Research on Minority and Women's Health with those under the Office of Science Training and Manpower Development. The merging of these two offices was logical since they previously worked together on a myriad of projects. The marrying of these two functions under one office has lead to greater efficiencies in the development of initiatives that embrace research and training. Dr. Milton J. Hernandez was named to head the new office.

OSPRT continues to administer the Bridging the Career Gap for Underrepresented Minorities Workshop and the Introduction to Biomedical Research Program (IBRP). In addition, OSPRT remains key in overseeing the reporting of the inclusion of minorities and women in phase III clinical trials and serves as the administrator of the NIH Ethics in Research Initiative.

The Director, OSPRT, has been instrumental in overseeing various collaborative funding efforts between NIAID and the NIH Office of Research on Minority Health and the NIH Office of Research on Women's Health. OSPRT is also involved in

supporting unique programs such as the Interamerican College of Physicians and Scientists (ICPS) and FEDIX/MOLIS, both described below.

Interamerican College of Physicians and Scientists (ICPS)

Recognizing that its mission can only be achieved through the interaction and participation of the minority scientific community throughout the United States, OSPRT is committed to an extensive outreach campaign that involves colleges and universities, medical centers, and professional organizations in pursuit of its goals. ICPS is the only national organization representing Hispanic/Latino physicians. ICPS had representatives on the NIH Minority Programs Fact Finding Team in 1992.

The official journal of ICPS, *MEDICO Interamericano*, is distributed monthly to 39,000 physicians in the United States and offers information on grants and contracts and professional opportunities for Hispanics/Latinos in academia, Government agencies, and the private sector. The outreach capabilities of ICPS can help increase the participation of Hispanic/Latino students in biomedical research and greatly expand the dissemination of information regarding minority issues and NIAID's role in addressing those in its scientific purview. NIAID continues to provide funding support to the ICPS Hispanic Youth Summer Program, which seeks to introduce Hispanic/Latino youth to careers in biomedical research through scientific seminars and field trips.

FEDIX/MOLIS

OSPRT also supports an Internet home page on the Department of Energy's (DOE) Federal Information Exchange (FEDIX). NIAID, DOE, and 18 other Government agencies participate in a research and development web site known as FEDIX/MOLIS (Federal Information Exchange/Minority On-Line Information Service, http://web.fie.com). The FEDIX portion of the system provides comprehensive information on Federal agency opportunities (i.e., grants, contracts, fellowships, equipment, and employment vacancies) to institutions of higher education nationwide. MOLIS is an information system that focuses specifically on Historically Black Colleges and Universities (HBCUs), Hispanic Serving Institutions (HSIs), and Native American Tribal Colleges and Universities. Along with minority scholarship and fellowship information, MOLIS contains up-to-date data on institutional and research capabilities for each HBCU and HSI, including more than 20,000 faculty profiles.

Another feature that makes the site beneficial is the Opportunity Alert feature. Users who register for the Opportunity Alert feature are electronically notified by e-mail when a grant, fellowship, or contract initiative in their area of interest is posted to the site. This eliminates the need for an individual to constantly check the site for the announcement of these opportunities.

NIAID pioneered the use of FEDIX/MOLIS at NIH for the purpose of (1) providing academic institutions, including HBCUs, across the United States access to NIAID's scientific agenda and funding opportunities; (2) assisting scientific review administrators in locating qualified minority scientists for review panels; and (3) meeting the House Appropriations Committee requirement to increase outreach to minority institutions. Although minority reviewers have been retained for some time, identifying qualified individuals has been difficult with the limited means currently available. The FEDIX/MOLIS database is a tool to increase greatly the ease with which this identification process can be accomplished and to expand the pool from which potential reviewers can be selected.

FEDIX currently hosts 20 Federal agencies, including many NIH institutes. In addition to displaying information about the agencies' research agendas and minority and student programs, the system includes access to HBCUs, HSIs, and Native American Tribal Colleges and Universities.

NIAID/Mali Medical School Minority Training Initiative

In early 1997, the NIAID Division of Intramural Research (DIR), the University of Mali Medical School, and the University of Maryland School of Medicine agreed that it would be beneficial to create

a program to provide training opportunities for minority students and young faculty in Africa. The underlying goal of the program would be to attract some of these individuals to careers in tropical medicine. The three institutions entered into an arrangement whereby American students would train in malarial research under Malian researchers at the Malaria Research and Training Center (MRTC) in Bamako, Mali. In turn, Malian researchers would be given sabbaticals to learn new research techniques at NIAID.

In December 1998, the Guest House was completed and ready for operation. It is located on the campus of the National School of Medicine of Mali and is immediately adjacent to the MRTC laboratories and the National Medical Library of Mali. The Guest House consists of a living room, dining room, kitchen, computer room/library, and eight bedrooms. Each bedroom is equipped with a computer as well. The computer room has two computers linked to the medical school LAN and the Internet. The Guest House serves as the base of operations for the program and is, indeed, a facility worthy of this important effort. It is situated within the medical school complex and is surrounded by an additional wall that is manned by a night guard to ensure the safety of the students. Mali is generally considered one of the safest countries in Africa; these routine precautions are designed to assure parents as well as student participants.

The MRTC staff, under the direction of Dr. Ogobara Doumbo, has organized a training program that can accommodate the various levels of students expected to participate. Among these are advanced undergraduates, graduate students, postdoctoral fellows, and junior or even mid-career faculty with a potential interest in research in tropical medicine. On the medical side, medical students, recent medical graduates, and junior medical faculty will be given the opportunity to participate in the training programs of the medical school along with exposure to work in the laboratory and in the field.

The training program emphasizes field research and opportunities to work in villages as part of ongoing MRTC research efforts for both science and medical fellows. NIH is preparing Mali as a major test site for malaria vaccines, and program participants will have an opportunity to take part in this important and exciting initiative.

In May 1998, the University of Maryland School of Medicine received funding through the Fogarty International Center to manage that part of the program responsible for promoting, recruiting, selecting, and posting the students and fellows in Mali. The recruitment effort is well underway. Initial announcements were sent to the directors of minority offices at 120 U.S. colleges and universities. The fellowships are not limited to minority students but minority students are encouraged to apply. In FY 1999, NIAID trained two researchers and three students have completed their fellowships at MRTC.

Las Hermanitas

In FY 1999, NIAID, along with the Office of Research on Women's Health, continued its support of the "Las Hermanitas" segment of their annual seminar for Hispanic teenage girls conducted by MANA, Inc. MANA is the oldest national organization for Hispanic-Latina women. The "Las Hermanitas" segment touches on the issues of sexually transmitted diseases, an awareness of symptoms of chronic diseases that are found disproportionately in the Hispanic population (i.e., diabetes, lupus, hypertension), and describes career opportunities in the sciences to which these young women can aspire.

NIAID Minority Scientists Advisory Committee

The NIAID Minority Scientists Advisory Committee (MINSAC) was established in FY 1991 by the Director, NIAID. In 1994, the Director chartered MINSAC as a standing committee within the Institute, and in FY 1995, MINSAC constituted and ratified its bylaws. MINSAC serves in an advisory capacity to the Director, providing advice on issues and concerns of the minority scientific community as well as suggestions on ways the Institute can attract and retain highly qualified minorities at all levels to its intramural and extramural programs.

MINSAC members, in conjunction with the NIAID Equal Employment Opportunity Advisory

Committee members, conveyed to the Director, NIAID, their concerns about the underrepresentation of minorities in the tenure, tenure-track, and postdoctoral positions within the Institute's intramural research program. As a result of discussions with the two groups, the Director has offered to provide the resources for the purpose of attracting and supporting underrepresented minorities in one tenure-track and two postdoctoral positions. These are competitive positions and are in addition to the total positions identified for this purpose within the Institute's intramural research program. MINSAC works with OSPRT and the Office of Special Emphasis in the recruitment of underrepresented minority postdoctoral applicants for these positions. The number of underrepresented minority postdoctoral fellows has grown from 2 in FY 1994 to 10 in FY 1999.

MINSAC also initiated the development of a minority constituency catalog, which includes minority scientists, institutions, and organizations. This catalog enables Institute staff to identify qualified minority scientists for participation in the NIH Peer Review System and is an interim step until a Minority Database System can be developed by NIH.

MINSAC also participates in the Institute's highly successful Introduction to Biomedical Research Program (IBRP), serves on various Institute ad hoc committees dealing with such issues as streamlining and affirmative action, and provides guidance on issues such as training and outreach.

MINSAC has also established a link with the NIH Black Scientist Committee in the sponsoring of key events, such as the John Diggs Memorial Seminar whose topics are geared to the academic level of NIH's Summer Research Program's student interns.

Bridging the Career Gap

In early FY 1993, NIAID recognized the need to increase the number of underrepresented minority investigators in the field of research. The result was an initiative designed for individuals currently funded by the Institute under various minority training and research supplemental awards to acquaint them with techniques to assist them in making that transition to the next step in a research career. The initiative, known as the Bridging the Career Gap for Underrepresented Minority Scientists, is a 2-day seminar that imparts information on how to select a mentor at each level in one's career and what opportunities and options are open in the field of biomedical research. It also provides participants with an opportunity to network with NIAID intramural and extramural staff members to make contacts within the Institute that they can draw upon in the future. It was designed to make them aware that NIAID felt it had a vested interest in their academic future. By establishing a bridging program, the careers of these young investigators could be nurtured, and the Institute would receive feedback on the effectiveness of these programs in attracting minority scientists to the NIAID research agenda.

In FY 1996, NIAID conducted an evaluation survey among the first two cohorts of the program to determine if their attendance at the seminar had been of any long-term value in propelling their research careers. Without exception, they reported that the program provided an excellent grounding in what to expect and how to make adjustments in their career plans, a sounding board of Institute staff to draw upon, and in general helped them make that bridge to a fulfilling career in biomedical research. NIAID also feels validation in the success of its "Bridge" program through its duplication by other NIH institutes.

The program is administered by OSPRT and is conducted with the assistance of NIAID scientific review, program, and grants management staff members as well as members from MINSAC. The fourth "Bridge" symposium was held in October 1999 and was attended by 34 individuals.

Introduction to Biomedical Research P rogram

The NIAID Introduction to Biomedical Research Program (IBRP) was established in 1979 to inform academically talented college juniors, graduating seniors, and first-year graduate or medical students from underrepresented minority groups about career opportunities in the broad field of biomedical research. This initiative grew out of the need to

increase the number of minority scientific researchers in this country. This program is also administered through OSPRT with the assistance of the Office of Special Emphasis.

This program consists of a series of small, scientific lectures, interviews, and tours of the renowned NIH campus. Students have the opportunity to discuss current research initiatives, scientific advances, and career concerns with NIAID's intramural scientists. The 4-day program is held annually in early February at the Bethesda campus of NIH. NIAID provides resources for the entire program, including room, board, and roundtrip airfare from the home institutions for the participating students. To qualify for IBRP, students must be American citizens as well as members of an underrepresented minority group such as African American, Native American, Alaskan Native, Hispanic/Latino, Asian, or Pacific Islander. The students, endorsed by faculty members of their respective colleges, schools, or universities, must have a grade point average of at least 3.0. Selection is based on GPA, faculty recommendations, and personal achievements. Annual attendance is limited to 60 students.

The majority of the program's speakers are from the intramural program but some are also drawn from extramural program staff, including several members of MINSAC, and from other NIH institutes to keep the program balanced.

In FY 1999, IBRP celebrated its 20th anniversary. We are beginning to see students from the early program come into their own, with several having received NIH grants, being tenured in academia, entering NIAID's intramural training programs, and joining the extramural staff.

Partnership P rogram

The Partners in Education Program, commonly known as the Adopt-A-School Program, was established in October 1983. The growing awareness and concern for the need of community involvement in education became clear. Businesses, Government agencies, and private organizations realized that something must be done about the state of education in America today and that the responsibility for the Nation's young people rests not only with parents but also with the greater community. School administrators identified four major areas that could benefit from outside involvement: institutional support, enrichment programs, extended service, and advisory service. The NIAID Equal Employment Opportunity Advisory Committee saw this program as a means to address the growing concern about the lack of minority participation in the biomedical sciences and forwarded to the Director, NIAID, the suggestion that the Institute become more involved in schools closer to home by adopting a local high school with the goal of providing scientific enrichment for its students. In fall 1991, NIAID and Dunbar Senior High School, located in the District of Columbia and noted for its pre-engineering and science program curricula, entered into a partnership arrangement.

In FY 1999, the Partnership Program has grown to five schools. In addition to Dunbar, NIAID has agreements with four Maryland Schools: Crossland and Friendly high schools and Carmody Hills and St. Thomas Moore elementary schools.

The program has enabled NIAID and the participating schools' officials to enter into a cooperative relationship that benefits both the schools and the Institute. As part of this program, students are exposed to a scientific environment in which they can nurture their interest in the sciences. Students, teachers, and administrators alike are developing a better understanding of the importance of research and the role of NIH scientists and support staff. The program affords participants the opportunity to see science in action, meet and consult with working scientists, participate in actual laboratory work to gain basic practical experience, receive supplemental instruction, and improve understanding and increase knowledge on various scientific subjects. NIAID offers resources that fall within the major support areas identified above: monthly lectures, mentors/role models, tutorial matching, library resources, incentive awards, workplace tours, faculty enrichment, and advisory services.

In FY 1994, NIAID's field laboratory, located in Hamilton, MT, undertook the adoption of two Corvallis County high schools, Hamilton and

Corvallis high schools. Because the student population is much smaller in this sparsely populated State, it was feasible for the Rocky Mountain Laboratories (RML) to take two schools under its wing. The program in Hamilton, MT operates much the same way as the program in Bethesda, MD: sending scientists into the schools and bringing students into the laboratories to participate in the conduct of research experiments. In addition, RML researchers have expanded their participation in the Partnership Program to include the mentoring of students and serving as judges for local science fairs. Approximately 20 RML scientists are participating in this program with approximately 100 students.

Biomedical Research After School Scholars

Scientists from RML have teamed up with local Montana schools to present an introduction to research programs for 7th and 8th grade students. The B.R.A.S.S. (Biomedical Research After School Scholars) Program was modeled after an NIAID program designed to introduce junior high school students to the fundamentals and relevance of scientific research in order to stimulate interest in science and encourage students to think of science as a career. The program consists of five lab sessions covering hematology, genetics, cancer, AIDS, and animal research. After scientists introduce a topic, students perform experiments designed to increase their understanding of the topic, as well as the nature of scientific research. The program concludes with a commencement ceremony at which students demonstrate experiments for their families and friends, and are awarded certificates and T-shirts for their participation in the program. RML is exploring the possibility of doing a mini 1-day version of the B.R.A.S.S. Program at schools in other regions of western Montana, which have predominantly Native American student populations.

III. Future Plans

Allergy, Immunology, and Transplantation

NIAID plans to vigorously pursue research in allergic diseases by fostering individual investigator-initiated research as well as providing support for multidisciplinary program projects and cooperative agreements dealing with mechanisms of asthma and allergic disease.

In early 2000, NIAID plans to review its Asthma and Allergy Research Program with an expert panel. This review will analyze the current portfolio and plans for future research and identify the best approaches to optimize the quality of research that NIAID supports.

Also in FY 2000, NIAID, in collaboration with the American Academy of Allergy, Asthma, and Immunology, and other professional allergy organizations, will publish clinical practice guidelines for the diagnosis, management, and prevention of allergic diseases and asthma.

NIAID anticipates that it will support a renewal of the Asthma and Allergic Diseases Research Centers with an RFA for FY 2001. This will continue to support multi-component projects consisting of basic and clinical studies concerning mechanisms of, and treatment and prevention of, asthma and allergic diseases. Furthermore, NIAID anticipates that it will support an extension of the Tolerance Network to studies of asthma and allergy by FY 2001.

The Institute will continue to support contracts for the development and use of reagents to prevent graft rejection and graft-versus-host disease. NIAID will also continue to fund clinical trials in transplantation to identify those protocols that optimize graft survival in solid organs and tissue. Moreover, NIAID will continue to fund the Adult and Pediatric Cooperative Clinical Trials in Transplantation with the goal of identifying those protocols that optimize graft survival in both adults and children.

Microbiology and Infectious Diseases

In the area of microbiology and infectious diseases, NIAID plans to continue its multidisciplinary effort in the conduct of science through basic research, targeted studies, and the development of innovative and new vaccine delivery techniques related to diseases and infections that disproportionately affect minority populations. Moreover, support for investigator-initiated research in areas related to minority health will remain a priority. Plans by research area include the following:

- NIAID will continue to support efforts to develop new tools to diagnose TB, new drugs or new ways to deliver standard drugs, as well as new vaccines to prevent TB. The Institute currently supports the sequencing of three mycobacterial genomes, a virulent clinical isolate of *M. tuberculosis*, *M. smegmatis*, and *M. avium*. Knowing the entire sequence of these genomes should contribute significantly to these efforts. NIAID will continue to support research aimed at developing the animal models needed in support of these research efforts.

- The NIAID Tuberculosis Research Unit contract will be recompeted and the Institute expects to make an award in FY 2000. NIAID will continue to emphasize the development of conjugate vaccines and synthetic peptides in addition to other preventive and therapeutic modalities effective against bacterial and viral pathogens.

- In the area of vaccines, NIAID will serve as the Investigational New Drug sponsor for a phase III efficacy trial in The Gambia utilizing a nine-valent pneumococcal conjugate vaccine administered in the same syringe as a DPT/Hib vaccine (Tetramune/WLVP). This trial is a two-arm,

double-blinded, placebo-controlled trial and will enroll approximately 50,000 infants over a 5-year period. The objective of the trial is to demonstrate improved child survival by impacting on pneumococcal disease. Enrollment is planned to begin in February 2000. NIAID, USAID, The Gates Foundation, and the British Medical Research Council will provide funding for this trial.

- Currently, licensed vaccines do have deficiencies as public health tools, particularly in regard to efficacy in very young infants. In developing countries, measles continues to be a deadly disease claiming more than 1.5 million lives each year. In those countries, infants are at greatest risk for serious disease and complications during the interval between loss of protective maternal antibody and receipt of vaccine at 9 to 12 months of age. Thus, internationally as we attempt to eradicate measles, there will be a need for an efficacious vaccine that can be safely administered earlier in infancy. Recently, NIAID has stimulated relevant research leading to the development of a number of potentially new measles vaccine candidates. Additionally, promising new animal model systems have been developed, and the specific receptor the measles virus uses to attach and enter human cells has been discovered. In the immediate future, research will focus on the preclinical development and comparative evaluation of these potential new vaccines, and the further establishment and definition of animal models.

NIAID has included "Emerging Infectious Diseases and Global Health" as one of the four cornerstones of its FY 2000 Strategic Plan. Research plans are aimed at enhancing NIAID's ability to predict, and thus prevent, conditions leading to disease emergence through a better understanding of the complex interactions among the pathogen, its environment, and its host(s) that influence disease emergence and transmission. The Institute's goal is to strengthen its ability to diagnose infectious diseases and detect pathogens in the environment; develop new or improved methods to treat illness, control outbreaks, and prevent epidemics; develop new strategies to control diseases that are reemerging due to drug or insecticide resistance; and to identify better control strategies for intractable infectious diseases that continue to pose challenges to the improvement of global health.

It is anticipated that in the next few years NIAID will place particular emphasis on the areas of genomics, bioterrorism, and infectious etiology of chronic diseases.

NIAID, in collaboration with several other NIH institutes, will sponsor a meeting in early FY 2000: *Hepatitis C in African Americans*. The central aim of the meeting will be to outline future research in an effort to elucidate why these differences exist and to spur the development of more effective therapies for all patients, but especially for African Americans for whom many therapies do not elicit a positive response.

Acquired Immunodeficiency Syndrome

In the area of AIDS research, NIAID will continue its efforts to develop innovative ways to augment minority participation in its clinical trials and epidemiologic studies and encourage the participation of minority investigators in all facets of basic and clinical research on HIV/AIDS. Specific future plans include the following:

- NIAID will continue to cofund meritorious, peer reviewed HIV/AIDS projects through the AIDS Infrastructure initiative of the RCMI Program, which is under the auspices of the National Center for Research Resources (NCRR).

- NIAID will continue to fund awards for the Adult AIDS Clinical Trials Group (AACTG) (RFA 98-013).

- NIAID will initiate a large-scale international trial of subcutaneous recombinant interleukin-2 in patients with HIV-1 infection and CD4+ counts of 300/mm3 (ESPRIT). It is anticipated that 4,000 patients in 18 countries will participate in this study.

- NIAID will develop and implement an AIDS vaccine communication campaign to increase awareness of AIDS vaccines before the initiation of a large efficacy study. This campaign will build support for HIV vaccine trials and improve recruitment and retention, particularly among minority communities and women.

- NIAID will fund the HIV Vaccine Trials Network (HVTN) and the HIV Prevention Trials Network. Both groups will recruit individuals at high risk for contracting AIDS.

- Within HVTN and in collaboration with other scientists, NIAID will study the scope and relevance of viral and human genetic variation in relation to vaccine development.